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THE MANAGEMENT OF THE MENOPAUSE: ARTIFICIAL AND NATURAL.[1]

By C. L. CHAPMAN,

Sydney.

"KNOWLEDGE comes but wisdom lingers" is a wise saying. In this age of scientific discovery, wisdom lingers too far behind knowledge. This is very true of the use of the modern œstrogens. These are powerful substances which science has given us, and harm has certainly resulted from lack of wisdom in their use. Excessive and too prolonged dosages have produced many bad results.

The Natural Menopause.

The natural menopause occurs on an average in the fifth decade, but may begin long before the age of forty years. Ovarian function fails, œstrogen secretion falls, and the gonadotrophic follicle-stimulating hormone is secreted in excess, unchecked by the rising level of œstrogen which occurs in the normal menstrual cycle. This unbalanced pituitary hormone produces the symptoms of the menopause.

All women reaching the correct age must submit to the menopause as a natural phase of their lives; 80% of women experience some symptoms at this time, but only about 10% severe symptoms. The most common symptom is "hot flushes". These may be so mild as to be almost unnoticed, or so severe as to make life intolerable. These flushes may be the only symptom, or they may be associated with sweating; and palpitations, irritability, giddiness, headaches and joint pains may also occur. In many cases there are most distressing difficulties in articulation, and sometimes a disturbance of continuity in trains of thought; a hiatus which causes great mental alarm may cause the patient to shout out. Whilst it is necessary to remember that these symptoms may occur before cessation of the menstrual periods, it is important not to attribute to the menopause every symptom in a woman aged between forty and fifty years. (A detailed account of the mental symptoms will be given by my colleague Dr. Sandes.) It should be emphasized that an exact history and examination should be made of menopausal patients. Many women will need only to be assured that their pelvis is healthy and their health good. Others are run down or suffer anxiety neurosis, and some have physical ailments which have no gynæcological basis. In some cases it is a good thing to use œstrogen as a diagnostic test.

What is then the problem of management? It is first of all to increase the 20% of women who experience no trouble. This is a matter of education—one must study the whole of the life of every patient. Try to keep the patient in the same activities. If she is in an occupation, let her remain in it. If she is idle, try to persuade her to occupy herself. Keep her at her golf, croquet or what not. Get her to maintain her sex life without fail, as nothing distresses a woman more at this time than to

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on November 26, 1953.

feel that she is of no use to her husband. The health of the genital organs should be maintained by vitamins, especially *C* and *D*. When there is failure in secretions, a suitable lubricant should be supplied. The next problem is to attend to the general physical health. Raised blood pressure will occur in at least 50% of cases. This blood pressure will be much better at sixty years of age than at fifty. Overweight will also require treatment. Proteins will be needed, but carbohydrates and fats should be greatly curtailed. A sodium-poor diet should be employed, as water retention tends to occur. A basal metabolic rate estimation may need to be made, and a suitable dosage of thyroid administered. Sedatives are useful, but should be carefully employed. Phenobarbital is in my experience outstanding. Keep the dosage low—quarter of a grain twice a day usually suffices. In combination with vitamin *B* complex it is more effective. Bromides should no longer be employed, as they are too depressant and their skin complications are too frequent.

Now we come to the specific treatment. As the symptoms of the menopause are due to the lack of œstrogen, its supply in some form is a specific remedy. The menopausal woman is far more sensitive to œstrogen than a normal woman, so we need only small doses. Quite small doses will produce toxic effects, such as nausea and vomiting, and higher doses will produce uterine bleeding, painful breasts and gain in weight. Uterine bleeding is a confusing symptom in a woman of cancer age, and mastodynia is distressing and also terrifying. It is well to remember that œstrogen is never present in the normal human body for more than a very few days without being balanced. Another point to remember is the varying degree of ovarian activity in different women after the menopause begins. The following preparations are at our disposal: (i) stilbœstrol, dosage 0·25 milligramme; (ii) dinœstrol (one-quarter the strength of stilbœstrol), dosage 1·0 milligramme; (iii) hexœstrol (one-eighteenth the strength of stilbœstrol), dosage 5·0 milligrammes; (iv) ethinyl œstradiol (twenty to twenty-five times the strength of stilbœstrol), dosage 0·01 milligramme. In my opinion the natural œstrogens are much superior owing to their power to produce increase in well-being; however, œstrone, the pure natural hormone, is so weak that when tablets are being used it is better to resort to ethinyl œstradiol. "Estigyn" and "Conestron" are available. I prefer tablets 0·05 milligramme being given daily for about ten days, and administration ceasing for about twenty days. If the patient objects to tablets, elixirs may be satisfactory. "Elixir Estigyn" is good in doses of one teaspoonful. "Linguets" I have not used, but they should be useful for the more intelligent patients. When should we use injections? Obviously when nausea and vomiting result from the tablets, and also, in my experience, when the patient complains of very persistent headaches (especially accompanied by a type of Ménière's syndrome) injection is essential. I give 20,000 to 50,000 units of œstradiol monobenzoate about every three weeks, always depending on the patient's own feelings. The smaller dose should be used to commence with and the effect carefully watched. I should be prepared to state that the only advantage in oral treatment during the menopause is the ease of administration. Tablets are really wasteful and uncertain. I have had no experience with the implantation method. In certain cases in which there are pronounced fissuring of the vagina and associated *pruritus vulvæ*, many physicians employ vaginal suppositories of stilbœstrol, combining them with the administration of tablets by mouth. I can see no logical reason for this form of treatment.

What is the trend and place of combined androgen and œstrogen therapy? Many papers have been written on this subject in the past few years. A. A. Loeser (1951), S. J. Glass (1950) and Greenblatt *et alii* (1950) have made lengthy and careful studies of this mixture of hormones. They all concluded that better results were gained than with one hormone alone. The effects are asserted to be as follows: (*a*) a more balanced physiological replacement; (*b*) a good effect from the androgens on the over-active gonadotrophic function of the pituitary; (*c*) beneficial trophic action on the vaginal epithelium. All these authors stress the tonic sense of well-being, and androgen in the mixture is said to allow a sharp reduction in the dosage. Androgens also improve the patient's psycho-sexual response, and as a result of the minimal dosage of œstrogen in the combination, withdrawal bleeding is very much reduced. It is held that androgens inhibit the mammary stimulation due to œstrogen and so counteract the tendency to painful breasts. My experience is small, but I advise the employment of combined hormones when symptoms due to the menopause associated with hæmorrhage are being treated.

The Artificial Menopause.

What special features are there in the management of the artificial menopause? There are two points which stand out: the artificial menopause is sudden in its onset and occurs in younger women. The symptoms are therefore more severe, more prolonged and more difficult to control. It is fair to say that the irradiation menopause is the most severe. Flushing, sweating, loss of libido and premature senile shrinking are special features of the artificial menopause. The two first-mentioned are the result of the sudden cessation, and the two last mentioned occur because the subjects are in full active sexual life.

With regard to the treatment, stress should be laid on preventive measures. In the surgery of pre-menopausal women, healthy ovaries should always be preserved. Radiation in castration doses should be avoided, and every effort should be made to preserve marital function. When a cervix is healthy, subtotal hysterectomy should be always employed, and when the cervix is unhealthy, enucleation operations should be practised rather than total hysterectomy. The latter should be reserved for malignant disease.

What special points are there in the hormonal treatment of the artificial menopause? The patients are younger and therefore larger doses can be tolerated, and ethinyl œstradiol becomes outstandingly better because of the sense of well-being it gives. Finally, psychological treatment is of great importance in these cases of artificial menopause. In occasional instances, such as widespread involvement of the pelvic fascia by endometriosis, œstrogen in any form is inadmissible, and psychological treatment and sedation are the only forms of treatment. A full life should be maintained, and especially should patients be encouraged to occupy their time either in jobs or by leading an active social life. They should be encouraged to maintain sexual activity in order to prevent the contraction of the vulva and vagina.

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THE MANAGEMENT OF THE MENOPAUSE.[1]

By S. G. SANDES,
Sydney.

THE fortress of the human personality is under assault from the cradle to the grave: in childhood, feelings of relative insignificance; in adolescence, doubts of capacity to face impending responsibilities; in adulthood, all the slings and arrows of outrageous fortune in both the material and spiritual fields.

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on November 26, 1953.

If the fortress is stoutly built, the scars of these assaults are negligible or mild; but if some weakness exists, and the outer defences are overrun by invading anxiety, then barricades are erected in the form of certain common reaction patterns of behaviour. These include all the well-known neurotic behaviour patterns, as well as generalized paranoid or depressive reactions, and the particular form taken in any individual case may be regarded as that individual's characteristic response whenever a stressful situation is encountered. As maturity passes into the involutional period, however, and life's sun inclines towards the west, stress becomes intensified with the realization of instinct decline, and the invader, anxiety, carries new weapons, particularly against the feminine sex.

Statistics as to the incidence of symptoms vary enormously. It seems probable that the majority of women do not suffer serious disability at the menopause. Many authorities quote 10% to 20% of women as having severe symptoms, but Weiss and English (1949) note 80% of women as having unpleasant symptoms requiring some form of medical assistance. Hawkinson, in a survey of 10,000 women, found 75% to suffer "distressing" symptoms in some form, and Israel noted the same percentage.

In an English series (Engle, 1944) of some 1200 women whose menstrual flow had ceased during the preceding five years, 62% complained of severe flushes, and 44% of severe headache.

Characteristic of the menopausal stress is its twofold nature. On the one hand, the endocrine system, with which personality itself is so very intimately linked, has its balance upset by reduction of œstrogens, and on the other hand the emotional stresses of the involutional period are many and searching.

I do not propose to discuss details of the hormonal changes; but it is well known that the general picture of this endocrine imbalance is the production of an over-responsive or sensitized sympathetic system. Upon this sensitized sympathetic system, via the hypothalamus, play a stream of anxiety-laden impulses of varying severity.

The characteristic vasomotor symptoms of the menopause due to the heightened activity of the sympathetic system are well known. Flushes, sweating, palpitation, irritability, headaches, paræsthesiæ, emotionalism and relative inability to cope with the usual stresses and strains of life may assail the hitherto reasonably well-adjusted woman.

In such a case œstrogens, particularly preparations of the naturally occurring follicular hormone, are likely to exercise a favourable effect; but this action is selective and is more or less constant only in the case of hot flushes and the atrophic changes which affect the genitalia. Dosage should be stabilized at the minimum necessary to produce results, and care is necessary in the presence of personal or family history of malignant disease.

When latent emotional difficulties are released, however, and when psycho-neurotic patterns are evident, the administration of œstrogens is likely to be not only inadequate but actually harmful, and may serve to stimulate libido and so activate psycho-sexual conflicts with which the individual may already be struggling.

It should be mentioned that the almost specific effect of œstrogens on some vasomotor symptoms such as flushes is questioned by some authorities. Pratt, in America (quoted by Weiss and English, 1949), has drawn attention to the suggestive effect involved in administering what is popularly regarded as a potent source of life force, and administering it, moreover, by injection into the body. He treated a number of women by injection with a preparation of natural œstrogen in oil, and treated a comparable group of controls by injection of the same oil without the œstrogen. He then sent his patients back to the practitioners who had referred them, and the practitioners' assessments as to improvement or otherwise showed a very close correlation for the two groups.

Reynolds (Buxton, 1944) selected for intensive investigation 18 women who complained of severe flushes only. He found that 11 did not respond satisfactorily to œstrogens, but did respond after psychic, economic or social conflicts were treated and adjusted. The relative preponderance of psychological conflict or endocrine imbalance in any particular patient showing vasomotor symptoms may sometimes be estimated by a therapeutic trial, in which œstrogens and inert placebos are administered on alternate occasions and the results assessed.

When anxiety is severe, and insomnia, palpitation and formless dread make life a misery, fears of insanity may arise and thoughts of suicide obtrude. This depressive colouring may be severe enough to suggest the use of electroplexy; but in these cases it is well to hasten slowly. In the case of more intelligent and sensitive patients particularly, the services of the psychiatrist with his electroconvulsive therapy machine are all too prone to represent a stigma, and the temporary relief of depressive colouring may be more than offset by the development of a refractory, secondary anxiety state due to such fancied stigma and fostered by the feline sympathy of the patient's friends and associates.

In place of electroconvulsive therapy, then, for such depressively coloured anxiety states, it is often well to place one's trust in explanation, reassurance, the judicious use of sedatives, manipulation of environmental factors with the assistance of the social worker, and supportive treatment generally, with administration of œstrogens when necessary for control of vasomotor symptoms.

A more serious mental disturbance is the generalized reaction, sometimes paranoid but more often depressive, which is met with in a variety of ætiological settings. The soil is fertile, whilst many seeds of anxiety are ripe to germinate at this season.

The menopause is the signpost that foreshadows many a threat to the female ego. To all it means the loss of reproductive power and thus the loss of woman's main biological purpose, and life without some purpose is nothing. To the spinster it marks the point of no return, and the final abandonment of her hopes of motherhood. To the mother it frequently coincides with a period when dependent children grow up and leave the home and no longer require maternal care. Husband or contemporaries and friends may die, and new friends are harder to make, whilst any economic difficulties become harder to combat. In addition, when emotional control is unstable, guilt feelings experienced earlier in life may be reactivated and add their depressive quota of attacks upon the ego.

Stern and Prados (1946) in a survey of gynæcological hospital out-patients classified as suffering from "menopausal syndrome", of whom 50% had had the services of the honorary psychiatrist, stated that practically all were reactive to obvious emotional problems involving commonly financial, domestic and sexual factors.

On the other hand, Farrar and Franks (1931) stated that climacteric depressions could be classified as roughly one-third reactive, one-third involutional melancholia in its strict sense and one-third endogenous depression.

To sample the position regarding psychotics in this State, it was decided to make a survey of all female patients within the involutional age group admitted to Callan Park Mental Hospital over a certain period. The age limits were set arbitrarily as between forty and fifty-five years at the time of admission to hospital. The total number of admissions in this age group was 76. From this total were eliminated those cases not connected with involution, such as mental defect, epilepsy, recurrences or exacerbations of psychoses present in earlier life, and certain organic conditions such as cerebral tumour, chronic alcoholism *et cetera*. When these had been eliminated there remained 54 cases in which frankly psychotic symptoms had developed for the first time within the involutional age limits I have mentioned.

Of these 54 patients, eight were still menstruating regularly at the time of their admission to hospital, and seven were showing menopausal irregularity, whilst in the remaining 39 patients menstruation had ceased on an average about four years previously.

The family history was regarded as indicating hereditary weakness if at least one close relative had been treated in a mental hospital.

Eleven patients showed an hereditary predisposition as judged by this criterion.

Physical disease, ill-health and trauma were prominent ætiological factors in ten cases.

The diagnoses fell into four main groups: (i) Reactive depressions (26) and manic states (two) accounted for a total of 28. (ii) Depressive states with pronounced paranoid trends accounted for eight cases. (iii) Cases in which the paranoid element was quite predominant numbered eight. (iv) Cases in which personality deterioration was present (the "late occurring schizophrenia" noted by many authorities) accounted for ten cases.

With one possible exception, mentioned later, no typically endogenous depressions were found, and no cases of involutional melancholia as judged by the usual criteria. The complete absence of these conditions with their very favourable prognosis may, perhaps, be regarded as a tribute to the vigilance of our colleagues in private psychiatric practice.

With the exception of some of the ten "late occurring schizophrenias", in practically all cases there were very obvious ætiological factors, and the psychoses were reactive predominantly (in order of frequency) to (*a*) bereavements, loneliness *et cetera*, (*b*) ill-health and physical disease, (*c*) financial insecurity and material worries, (*d*) conscious guilt over previous sexual peccadillos.

The prognosis was found to be as expected—namely, good in the predominantly depressive conditions, moderate to poor in paranoid conditions and very poor in schizophrenic types of disorder.

The question of the artificial or surgically induced menopause is more the province of my fellow speaker in this discussion; but a few points in connexion with it emphasize the complexities of the menopausal problem: (i) some younger women undergoing a surgical menopause have only mild symptoms; (ii) some exhibit the typical menopausal vasomotor syndrome; (iii) a few have no symptoms at the time, but exhibit the menopausal syndrome when they reach the involutional period of the late forties, which may be many years after the removal of their ovaries.

In this small survey, six cases were complicated by previous operations on the generative organs. Two of these operations were apparently hysterectomy only and had been performed respectively one year and two years before admission to hospital on women who exhibited severe depressive psychoses. One patient with a paraphrenic psychosis had had uterus and ovaries removed fifteen years previously. One patient had a history of anxiety state of gradually increasing severity since castration three years before, and this culminated in an acute confusional psychosis. One patient was said to have been "never the same" after castration ten years before and was admitted to hospital with severe and irreversible mental deterioration.

The remaining case may be mentioned a little more fully:

X., a married woman, mother of two children, Roman Catholic, was admitted to hospital at the age of forty-three years. There was no family history of mental illness. She had been educated at a convent, had married at the age of twenty years, and was reported as a bright, jolly, affectionate type, although "a bit of a worrier". Her marital and social adjustments had been apparently satisfactory until about three years before her admission to hospital, when, at the age of forty years, she was noticed to become increasingly meticulous, tidy and conscientious, worked all day, never leaving the house, and suffered from severe "hot flushes". She was given "gland injections and tablets" by her medical attendant and improved considerably, being now bright and cheerful and wanting to go out "all the time". About one year later (two years before her admission to hospital) she had uterus and ovaries removed for reasons not adequately elicited in the history.

Three weeks before her admission to hospital she contracted influenza, and her mental condition rapidly deteriorated to a stage of confusion and complete mental disorganization, and she was certified as insane. As is to be expected in cases in which the pre-psychotic personality has been fairly good, and in which the onset of the psychosis has been marked by rapid disorganization of mental function, she responded well to electroplexy and left hospital within a few weeks.

Such cases demonstrate the way in which the underlying psychological attitudes and personality trends may be activated and released both by glandular imbalance in the involutional period and also by bodily infections.

An interesting line of research into the interaction of endocrine and psychological factors was opened up by the work of Benedek and Rubenstein (quoted by Weiss and English, 1949). They endeavoured to correlate on the one hand somatic findings, such as the basal metabolic rate and results of vaginal smear examinations, and on the other hand psychological attitudes as assessed simultaneously and independently by a short modified psychoanalytical technique. Their findings were tentative, but tended to show that during the phase of follicular ripening the psychological material was dominated by positive libidinal interest directed towards the opposite sex, whilst in the stage of progesterone dominance the subjects were inclined to be more passive and receptive, and a disposition to impregnation, child-bearing and child-caring was reflected in the psychological material.

Endocrine Therapy.

When the endocrine therapy of the menopausal period is considered, the following points seem on the way to general acceptance.

The only definite and pathognomonic signs of œstrogen deficiency, apart from amenorrhœa, are the co-called hot flushes and atrophic changes in the genitalia. Œstrogens will generally (though not invariably) relieve these; but in spite of many efforts no correlation has as yet been established between frequency or severity of flushes on the one hand and œstrogen levels in the body on the other hand.

The work of Pratt and Thomas (1937) with carefully disguised placebos showed that the majority of their patients were benefited to a significant extent by such diverse substances as theelol, phenobarbitone and lactose when these were administered in identical form.

In the purely vasomotor syndrome, especially in the reasonably well-adjusted woman, œstrogens relieve symptoms, sometimes dramatically, and increase the sense of well-being; but superadded anxiety symptoms will not necessarily be relieved. Œstrogens will not dispel the worry as to where the next rent is coming from, nor will they assuage the pangs of a guilty conscience.

Careful physical examination is necessary to ensure that such conditions as cardio-vascular degeneration with hypertension, arthritis and menorrhagia are not dismissed as temporary functional accompaniments of the menopausal period. Œstrogens will not halt the inevitable onset of change and decay in body tissues.

Malamud *et alii* (1941) have drawn attention to the similarities of the adolescent and involutional periods:

> Both are transitional stages and as we seek to prevent adult personality disorders by understanding the problems of adolescence, so we must understand the problems of the involutional period in order to prepare for adjustment to the pre-senile and senile periods.

With our increasing life expectancy, this transition stage gains added importance. We should be active in disseminating, where possible, the seeds of education in mental health, so that we may do our share to dispel widespread popular fallacies such as those connected with the mysterious "change of life".

Conclusion.

In dealing with our patients who experience difficulty in passing through the menopausal and involutional periods, our aim, in addition to dealing with individual problems, should be to reinforce the ego by increasing the sense of self-esteem and by finding avenues of self-expression which will serve to provide friends for the friendless, oppor-

tunities for service to the self-centred, and pecuniary assistance to the financially embarrassed. The implementation of these aims will tax the resources of the physician, the psychiatrist, the spiritual adviser and last, but far from least, the almoner and social worker.

To sum up: œstrogens in general appear of value mainly in the alleviation of "hot flushes" and of atrophic changes in the genitalia. When emotional disturbance is pronounced and when mental conflict is uncovered, they may be not only ineffective but actually harmful.

The anxiety states and mildly depressive neuroses of the menopausal and climacteric period, particularly in the more intelligent and sensitive type of patient, are often best treated with explanation, reassurance, environmental manipulation when practicable, and the judicious use of sedatives and œstrogens.

When psychoses occur, they are likely to be predominantly reactive to loneliness, bereavements, financial difficulties, conscious sex guilt or failing physical health, and their prognosis with the drastic therapies varies roughly as the ratio of the frankly depressive to the frankly paranoid elements in the clinical picture. The services of the social worker are invaluable after remission.

In conclusion, let me repeat the words of the eminent gynæcologist quoted by the late F. A. Maguire at the end of an address on a similar subject. He said: "Always be kind to women, they have such a lot to put up with."

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EVALUATION OF LITHIUM IN TREATMENT OF PSYCHOTIC EXCITEMENT.

By B. GLESINGER,

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THE work of Cade on the treatment of psychotic excitement with lithium salts stimulated a series of tests with lithium on 104 patients and prompted the present study.

A mental hospital, with many hundreds of patients with chronic mental disorder and with the incessant trouble of excited patients, is in very great need of a sedative with little or no narcotic qualities. Electro-convulsive therapy, excellent and helpful for fresh patients, is dreaded by many patients and is frequently less effective in the treatment of patients with chronic illness. The increasing of its efficacy necessitates its application in higher doses (units of current) or at shorter intervals. This in itself produces the often mentioned dulling effect which one would like to avoid. In many cases sedatives are found wanting in their effects, unless the patient is subjected to narcosis treatment.

The results obtained by Cade with lithium appeared encouraging and nearer to the solution of the problem of ideal treatment. The criteria of an ideal medicament should be as follows: (*a*) it should preferably be tasteless or not deterrent in taste, (*b*) it should be harmless, (*c*) it should have sedative qualities, (*d*) it should have few narcotic side-effects, (*e*) it should be applicable for a long period.

Although most of the patients referred to by Cade were suffering from chronic mania or recurring manic episodes, it was obviously natural—as already suggested by Cade—to try lithium on all restless, excited, troublesome patients, and with the sedative effect of lithium in mind, also on those who suffered from hallucinations and delusions if these were the underlying cause of their restlessness.

Experience has taught that lithium citrate, while soluble, was much to be preferred to, and safer than, the chloride in daily distribution to patients. The chloride, a suspension, demands reliable and exact shaking of the medicine bottle so as not to run the risk of an overdose or underdose. Twenty grains of lithium citrate were administered for a period of seven to twelve days, in some cases even to fourteen days. Then doses were reduced to 10 grains three times daily, and patients were left on that dosage for a month or longer before further reduction to 10 grains twice daily. For chronically ill patients with a stable course this dose appeared to be sufficient for months, while patients with recurring impetuous, manic or hypomanic conditions or even only with periodically appearing states of restlessness and hyperactivity needed a continuous dose of 10 grains three times a day. A maintenance dose of 10 grains once a day, administered indefinitely, was found to be effective for a minority of patients with less manifest symptoms.

Many good results were achieved with lithium, but its toxic quality was also encountered. All toxic effects occurred at the beginning of our experiments with lithium, a result of the selection of unsiutable patients for this treatment and of deficiency of sodium chloride in their diet. Figure I shows our results in general.

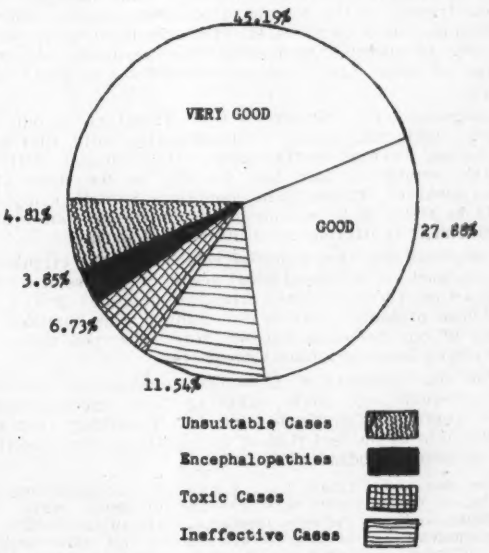

FIGURE I.

The results in the various reaction types were as follows:

1. Of seven patients with recurrent mania, one responded very well, four responded well and two failed to respond.

2. Of 14 manic-depressives, four responded very well, six responded well and four failed to respond.

3. Of 39 excited schizophrenics, 23 responded very well, eight responded well and eight failed to respond.

4. Of 12 hebephrenics, five responded very well, four responded well and three failed to respond.

5. Of six epileptics, three responded very well, one responded well and two failed to respond.

The remaining 26 cases represented various groups of reaction types—for example, paraphrenia, psychopathy, post-traumatic organic dementia, post-encephalitic brain lesion, general paralysis of the insane, senile dementia, katatonia, alcoholism, mental deficiency and alcoholism, organic confusional insanity, *et cetera*. In view of the small number of patients (one to three) in each of these groups, the percentages of success and failure respectively are not given here, but it is noticeable that the average of response in these groups even surpassed that of the schizophrenia group.

The calming effect on maniacal, excited, hyperactive and restless patients was most satisfying and appreciable. It was first noted after one and a half to two weeks (in some rare cases even earlier), was fully developed about three to four weeks after the commencement of lithium treatment, and lasted three to six weeks, in some cases even eight weeks, after its withdrawal. In regard to symptoms it deserves to be noted that all kinds of manifestations were beneficially influenced, from hostility to hypochondria, and from ideas of persecution to obsessions. Restlessness, confusion, irrationality, hyperactivity, agitations, hallucinations, delusions, impulsive actions and garrulity were the manifestations most relieved. Yet even dull, destructive, blocked solitary and morose patients have changed their personality, and one man who, solitary and moody, had always defied medical officers, started to converse in a friendly way.

Seven patients (6·73%) amongst those who have not responded to lithium developed gastrotoxic symptoms, and four (3·85%) nervous symptoms. There are clear distinctions between these two precisely defined groups. The symptoms with relation to the central nervous system in order of appearance are as follows: tremor of fingers and hands, tremor of the tongue, depression, apathy, difficult mentation, muscle twitches, slight ataxia, blurring of vision, slurring of speech. Nystagmus was regularly observed. In the advanced state, convulsions, coma and death may occur.

Symptoms with relation to the alimentary system are nausea, anorexia, gastritis, occasionally mild diarrhœa, feebleness, mental indifference with reduced activity. Gastric symptoms may last for five to ten days after withdrawal of lithium, and doubtless gastric symptoms could be followed by symptoms of central nervous system involvement if lithium medication was continued.

Symptoms are also reported relating to the circulatory system, such as depressed heart action, weakness of cardiac contraction (with possible arrest in diastole) and a fall in blood pressure. The last-mentioned was manifest in many of our patients, but we never observed the other depressive heart symptoms mentioned.

The four patients with central nervous system signs were beyond any doubt suffering from encephalopathy. This disquieting thought becomes less disturbing when seen in the light of the fact that all four patients were receiving a diet poor in sodium.

One case ended fatally. A., a male patient, aged forty-five years, a hebephrenic, was violent, interfered with other patients, and was restless, confused, dirty in his habits, and unmanageable. Physically he was slender and rather delicate, but of fairly good health. Lithium citrate treatment was initiated on February 4, 1950, with 20 grains three times a day. The first improvement was noticed on February 16. No toxic symptoms of any kind had been recorded by then. On February 17 he was slightly depressed and the lithium dose was reduced to half an ounce (10 grains three times a day. On that day the patient had lost his restlessness, violence, impulsion and confusion. Lithium therapy was discontinued at 8 p.m. On February 18 he became ataxic and unsteady, but improved later in the day and walked very well. Later in the evening he had an epileptic fit, which was followed by two others during the night. On February 19 he was confused and refused to take food, so he was tube fed. His condition improved slightly up to February 24; however, tube feeding became impossible owing to continuous intraoral (tongue) and intranasal counteractions. Treatment consisted in the administration of analeptics, oxygen *et cetera*. Incoordination of various muscle groups and general weakness were noted. He died on March 1. The post-mortem findings were as follows:

Macroscopically thickening of arachnoidea of parietal lobes. Otherwise N.A.D. Histological findings: Marked segmentation of cardiac muscle-fibres, moderate interstitial fibrosis. Some pyramidal cells of cortex show loss of Nisl substance and nucleus. Many microglial cells round them. Lymphocytes and polymorphs round hyperæmic capillaries; query encephalitis type. Congestion of kidneys.

The first symptoms of the three other encephalopathy patients appeared on the sixth, tenth and twelfth treatment days respectively. These symptoms were comparatively mild, but notwithstanding typical—general weakness, lethargy, drowsiness, slightly slurred speech, nystagmus, and in two cases also slight ataxia. Only one patient had a slightly raised temperature and only one complained of headache. There were no striking changes in the pulse and respiration rates. The deep reflexes were not affected during the first days of these toxic effects.

In spite of the fact that these cases were discovered early enough for the symptoms to be combated, their discovery was, of course, embarrassing, and to cope with the situation instantly and effectively and to avoid further progress of the toxic state, immediate treatment was introduced and lumbar puncture was omitted. "Cylotropin", 10 cubic centimetres, was administered intramuscularly for three days in succession. All signs including nystagmus disappeared on the fourth day, and on the fifth day the patients were their former selves—brighter, active and again interested in their surroundings. The action of "Cylotropin" in these three cases being satisfactory, it was intended to examine the cerebro-spinal fluid for diagnostic purposes before starting treatment in the next case, but fortunately no more encephalitic symptoms in lithium-treated patients have occurred since the early months of 1950. In the case which ended fatally no "Cylotropin" treatment was given, since I was on holidays when the patient's condition began to deteriorate.

Some weeks after the initiation of lithium treatment it seemed advisable to investigate the activity of the kidneys in view of the prolonged treatment with large doses of a metal salt. A parallel with the kidney-damaging metals and their salts, such as mercury, arsenic, copper, antimony, lead, bismuth, gold, zinc, chronium, thallium, uranium and potassium bichromate was also obvious.

Since albumin was detected in the urine of several patients, all of them were subjected to extensive examinations in relation to the appearance of albumin, also in different postures and at various hours of the day; urine sediments were examined regularly and blood samples for urea estimation were taken occasionally (Harrison, 1943; Sahli, 1924).

The following exposition deals with those patients whose urine was free of albumin some time before the introduction of lithium treatment, except for patients with orthotic albuminuria. Albuminuria had been detected previously in a few of these orthotic types, and frequently repeated examinations have shown these to be cases of orthotic albuminuria.

Moderately severe albuminuria was detected in 23 cases, which amounted on the average to about 0·03% of protein or less; most of the patients excreted only a minute or faint amount of albumin. Examination of the sediment of all these specimens of urine gave negative findings. Erythrocytes were never found, and single casts were seen only very rarely. No spermatozoa, mucus or proteinurias of other kinds were present. The blood urea content was normal and the blood pressure remained low. Once only did I come across some crystals, which I had never seen before and never saw again in all these many hundreds of samples. I was unable to find pictures of any similar crystal in any of the standard books. Their shape resembled that of sulphanilamide crystals.

It was revealed in the course of the observation, which extended over a period of three years and three months, that some patients excreted albumin for a limited time during their lithium treatment and some after its termination. Yet there was, in some cases, a break in the continuity of albumin excretion; it appeared intermittently

before it finally disappeared. The excretion of albumin lasted on an average from several weeks to two months; in three cases it lasted for five or six months. Most of the patients with albuminuria were finally restored to normal, except for three patients, of whom one suffers from orthotic albuminuria most probably aggravated by lithium.

Information on 23 cases of albuminuria out of 104 lithium-treated patients is set out below. Patients with preexistent albuminuria, phosphaturia, oxaluria, nephrolithiasis and uratic diathesis with transient albumin excretion are excluded.

Group I: Seven patients (30·43%) had albuminuria during lithium treatment for a limited time (several weeks to two months); one with the orthotic type is included.

Group II: Seven patients (30·43%) had albuminuria after the termination of lithium treatment and for a limited time only (several weeks to two months); two with the orthotic type are included.

Group III: Two patients (8·69%) had albuminuria during treatment and for some time after (several weeks). In one case albuminuria appeared intermittently; it appeared twice within six months, but never later, in spite of the continuation of lithium treatment for one whole year.

Group IV: Four patients (16·79%) had an increased albumin excretion during lithium treatment and persistent albuminuria for a rather long period afterwards. All cases in Group IV are cases of orthotic albuminuria.

Group V: Three patients (13·04%) had albuminuria after the termination of lithium treatment and persisting for a long period; one with the orthotic type is included.

Amongst these 23 cases were eight of the orthotic type proved in countless reexaminations and investigations, in which the albuminuria was aggravated by lithium. These patients excreted slightly more albumin during treatment or for a limited time afterwards, while their albumin excretion dropped to lower amounts several months after the conclusion of the lithium medication.

The albuminurias in Groups I to IV were not coexistent with other pathological symptoms, and sooner or later this particular pathological condition was reduced to normal.

I regard only two cases of Group V as significant of persistence of very slight to moderate albuminuria and more or less slight damage to the kidneys. The symptoms have persisted now for two and a half and three years respectively. Both patients excrete albumin irregularly and erratically.

One patient, B., a male, aged twenty-four years, has a normal urea excretion with a clearance of 98% within three hours and a blood urea content of 61 milligrammes *per centum*. His urinary sediment is normal; his blood pressure is 110 millimetres of mercury, systolic, and 55 millimetres, diastolic. There is an improvement noticeable; while tests still showed a comparatively high albumin excretion some months ago, the test results can now be marked on some days as "trace" or even "faint trace". For a long period he had a pronounced isosthenuria, which has most strikingly diminished, and concentration can be regarded as normal at present, while dilution figures are still erratic and comparatively high. He is evidently at the turning point.

The other patient, C., a male, aged twenty-two years, has a urea excretion of only 2·17 grammes with a clearance of 68% within three hours or 87% in four hours, and a blood urea content of 79 milligrammes *per centum*. Concentration and dilution of urea are present, but concentration appears to be irregular. Excretion is slightly impaired and prolonged. Examination of the urinary sediment reveals no abnormality. The blood pressure is 135 millimetres of mercury, systolic, and 65 millimetres, diastolic.

Comment.

Dosage, Excretion, Toxicity.

Numerous mineral waters—mostly carbonic acid water from medicinal springs—contain lithium in very small amounts, up to 51 milligrammes of lithium ions per litre. The amount taken by a visitor at a spa by no means exceeds 0·1 gramme per day. Results produced after a cure of two to four weeks' duration are stimulation of stomach secretion, reduction of mucus, favourable influence on motility, an increased turnover of nitrogen-containing tissue elements, acceleration of metabolism, and increased excretion (Strasser). It is a fact that thousands of people yearly are greatly assisted or cured by these homœopathic doses.

Pharmacopœias of various countries naturally list higher doses. The Austrian pharmaceutical codex (Tappeiner, 1923) states the dose of lithium carbonate as 0·1 to 0·3 gramme. The English codex (Martindale, 1952) limits the dose of lithium chloride from five to 10 grains (0·3 to 0·6 gramme), of lithium carbonate from two to five grains (0·13 to 0·32 gramme), of lithium citrate from five to 10 grains (0·32 to 0·65 gramme). According to Potter the doses in the United States of America are for lithium carbonate two to 15 grains and for lithium citrate five to 20 grains. These higher maximum limits customary in the United States of America may have induced chemists in the United States of America to use higher doses of lithium chloride for table-salt substitutes, which have caused several severe poisonings. Corcoran *et alii* have reported seven cases with two deaths, Hanlon *et alii* three cases and one death, Waldron two cases, Stern one case.

Noack and Trautner refer to the peculiarity of lithium bromide used against epilepsy on the one hand and its liability to cause convulsions on the other hand. There is an answer to it in the Pharmaceutical Codex, which states as its safe doses five to fifteen grains. With the warning of 15 grains as a maximum in mind, the rarely exceeded average of a single dose would be 10 grains; while, to produce the desired effect of lithium on psychotic excitement, 20 grains of the citrate are used for seven days and longer, which is just on the verge of toxicity. Apart from that it is an axiom of medicine and homœopathy that small doses cure, larger doses poison and the largest bring about death. We found a dosage of 20 grains three times a day of the citrate toxic only if given for longer than three to fifteen days according to the individual compatibility. Smaller doses, 10 grains three times a day, were given to patients for up to eight months without even the slightest toxic symptoms being caused.

Good found that lithium is excreted into the saliva, stomach and bowel and chiefly by the urine. Excretion is slow. Lithium has been detected twenty-three days after administration has been stopped. Gastro-enteritis is caused by excretion through intestinal walls. Noack and Trautner believe that secretion lasts ten days from a single dose and fourteen days from a three days' course. These seemingly diverse statements do not imply a difference in the results of investigations, since Good may have investigated patients on lithium treatment of longer duration than three days. However, both findings show a remarkable lithium retention—that is, an exceptionally slow secretion; hence the accumulation of toxic substances which, when released, account for the symptoms of poisoning which develop so suddenly and persist for so long.

As to the question of retention, it is of some interest that Hunter and Aub studied the effect of parathyroid hormone on the excretion of lead and calcium in patients suffering from lead poisoning. It is highly probable that in a similar way hormonal glands rule retention, excretion, ionic composition and osmosis of lithium in the body.

Various hypotheses exist as to the mode of the toxic action of lithium, though none seem to meet the case. Kent and McCane ascertained by tests and experience that lithium replaces sodium in the extracellular fluid, and its presence facilitates sodium depletion of the body. Its slow excretion and retention become a potential danger; yet its toxicity is conditionally dependent on individual tolerance. It appears that the places of action and points of attack of lithium are individually different. Out of seven patients with gastrotoxic symptoms, only one had albuminuria, and only one out of four encephalitis patients. One patient had been on lithium treatment twice with an interval of eleven days. The first time he took lithium well, but had gastrotoxic symptoms twenty-eight days after the second treatment course had started. One of the four encephalitis patients had been on lithium treatment three times, the first time for twelve weeks with excellent result. After an interval of five weeks he took lithium again and suffered

slight gastritis, which lasted for several days. After a further interval of fourteen weeks he was started on lithium treatment once more, and developed symptoms of encephalopathy within ten days.

Lithium poisoning can take a very drastic course if it is not detected in time, and especially if it is connected with symptoms involving the central nervous system. In one of our cases toxicity developed after three days. Although we were surprised at the beginning by rapidly developing toxic symptoms in several cases, and by one fatality which occurred more than three years ago at a time when the lithium-sodium relation was still unknown to us, we now hold that symptoms of toxicity are quite characteristic and cannot be overlooked when the patient is seen and observed daily. There is no necessity to measure or control lithium excretion by complicated chemical methods or to determine the plasma content. This refinement can be reserved for institutions with appropriate facilities. Lithium treatment can be carried out in any hospital safely and even at home under supervision.

Indispensable conditions for the safety of this treatment are as follows. (i) The right patient must be chosen. Abnormally quiet, inactive, depressed, enfeebled patients must be excluded. (ii) The daily sodium chloride intake must be increased during lithium treatment.

At the appearance of toxic symptoms or during an intercurrent disease, the following must be done: (i) lithium medication must cease at once; (ii) saline infusions must be administered; (iii) diuretics, diaphoretics and laxatives must be used to promote excretion; (iv) "Cylotropin", 10 to 15 cubic centimetres, must be given intravenously or intramuscularly once a day on three or four days in succession; (v) sodium thiosulphate, or BAL, or both, must be given intravenously.

Encephalopathy.

To my knowledge, only one pathological report is available from the lithium cases so far published. I shall, therefore, omit the histological classifications (whether vascular, degenerative, or exudative encephalopathy *et cetera*), and will refer in the subsequent exposition solely to clinical symptoms for purpose of comparison with other known cases of lithium encephalopathy in order to prove their origin from and identity with the action of lithium (Brain, 1951; Cecil and Loeb, 1951; Glesinger, 1927; Hammon, 1943; Tidy, 1928; Mohr and Staehelin, 1929; Robertson, 1952; Shiels, 1952; Southard and Hunt, 1928; Volhard, 1929; Weller and Christensen, 1925).

The initial symptoms of encephalitis are not different from those of lithium poisoning as known to us and represented by the description of Noack, Roberts, Stern, Corcoran, Waldron, Cleveland and others. In cases of the severe European encephalitis epidemic the same initial manifestations were observed. Only in the course of the disease were there symptoms of paresis in the lethargic form, and of characteristic choreic movements with twitching and violent contractions in the myoclonic form followed by all kinds of signs, depending on the seat of the encephalitic foci. Graeme Robertson during the Murray Valley encephalitis epidemic found anorexia, headache, vomiting, drowsiness, lethargy, irritability, giddiness, and in younger patients convulsions as initial symptoms. The same symptoms are mentioned by Brain, Economo, Osler, Tidy and countless others.

The histological findings in our case mentioned above are those of some kind of encephalopathy, and there is little doubt that Roberts's case (and probably also those of Stern, of Corcoran and of Hanlon) were likewise encephalopathies, with such extremely small macroscopically invisible hæmorrhages that only a microscopic examination could establish the diagnosis. Incidentally, two metals and alcohol are recognized as causes of encephalopathy closely resembling the clinical picture of some types of encephalitis. (i) Lead produces *encephalopathia saturnina* (Brain, 1951; Tidy, 1928; Mohr and Staehelin, 1929; Shiels, 1952; Volhard, 1929; Weller and Christensen, 1929), with headache, vertigo, convulsions *et cetera* producing selective degeneration of ganglion cells of the cerebral cortex and of the anterior horn (Mayer, Brain). (ii) In cases of another encephalopathy caused by a metal compound, arsenobenzene, Brain describes perivascular hæmorrhage and areas of necrosis and demyelination. With regard to convulsions it is known that encephalitic foci with even small hæmorrhages situated in or near the grey matter are likely to produce fits, though this may occur rarely.

Many patients with the lethargic encephalitis type of condition had a very slight rise in temperature. It is not to be expected that conditions caused by poisons would produce a higher temperature; on the contrary, terminal hyperpyrexia points, in the absence of any macroscopic pathological findings, to a cerebral origin and hardly can be regarded as a symptom of poisoning alone.

Further to my assertion that certain described manifestations of lithium poisoning can be traced to cerebral causes, and also that they are manifestations of central nervous system involvement and not of general poisoning, I wish to make the following points. (*a*) A certain difficulty in swallowing (Stern) by otherwise hyperactive muscles suggests a bulbar symptom rather than a local pharyngeal muscle weakness. (*b*) The description by Stern, "both of his great toes assumed a position of dorsiflexion", can be read as a Babinski phenomenon, which is again a cerebral sign, uncommon in general poisoning. (c) Poisons attacking the peripheral muscles and causing general weakness would be likely to cause hypoæsthesia, lowered muscle tone and lessened muscular irritability; while hyperæsthesia, muscular hyperirritability and multiple myoclonus with simultaneous weakness, apathy and lethargy suggest a cerebral initiation of muscle symptoms. In cases of involvement of the brain manifestations will depend on the localization of the focus. In Stern's patient with Babinski's sign and extreme hypersensitivity and painful irritability of the skin, multiple cerebral foci may have been present—central and cortical foci situated close to the meninges. (*d*) Finally, much will depend, in general, on the phase and progress of the disorder. Disorders not yet fully developed and still in their initial state are expected to cause hyperæsthesia, hyperirritability and increased myotonus. Fully developed conditions, having caused pathological changes, will rather produce hypoæsthesia, lowered myotonus, hypoirritability and impairment of tendon reflexes.

A further point I wish to raise in favour of the diagnosis of encephalopathy is the observed nystagmus in our cases (Brain, 1951; Browne, 1951; Cruickshank, 1952; De Jong, 1946; Howells, 1952; Tidy, 1928; Lindsay, 1951; Reed *et alii*, 1951; Warren *et alii*, 1950). This symptom is found in a multitude of pathological states, but can be traced back ætiologically to cerebellar, cerebral or labyrinthine lesions, or to a weakness in relation to the eye and eyesight (ocular and optokinetic causes), or to chemical and toxic agents—for example, botulism and alcoholism. Neither of these two last-mentioned conditions produce in the central nervous system the symptoms peculiar to lithium. The symptoms of our three patients were also not related to any of the other conditions—cerebellar, labyrinthine or ocular—which have nystagmus as one of their leading signs. But they were distinctly of cerebral origin. From this can be inferred that these typical manifestations in our patients (and in those cases of lithium poisoning with nervous symptoms described by others) in conjunction with nystagmus strongly suggest encephalopathy; it can even be said that nystagmus, a very constant attendant of encephalitis, added to the noted other manifestations confirms the diagnosis of encephalopathy.

Another leading equally important sign is ataxia developing in lesions of the cerebellum, spinal cord, brain stem or cerebral hemispheres. Ataxia was observed in some of our cases and mentioned by Cade, by Roberts and by Noack *et alii*.

The fact that lithium is found in higher concentration in muscle than in liver (Waldron) does not justify any conclusion that it is a general muscle poison, since nothing is yet known about its concentration in the brain. It was

also stated (Talbott) that excessive sedation, digitalization, unrelated infection, thrombo-embolic phenomena or the natural progress of cardiac disease may cause the same symptoms as lithium poisoning.

It is doubtful whether the cerebral symptoms noted in our patients who also showed nystagmus and ataxia can be attributed to any of the foregoing conditions apart from thrombo-embolic phenomena.

Albuminuria.

Waldron in his exposition on lithium intoxication stated in 1949 that impairment of kidney function was suggested (Allen, 1951; Ashburner, 1950; Bell, 1950; Bing, 1936; Cecil and Loeb, 1951; Harrison, 1943; Isbister, 1951; King and Gronbeck, 1952; Platt, 1952; Salt and McMenemey, 1949; Smith, 1951; Volhard, 1929; Whishaw, 1950).

In our 20 cases in Groups I to IV the albuminuria was moderate (±) to extremely light and was not associated with any other renal symptom. If all five groups are considered, its duration was in 18 cases up to two months only, in two cases five months, in one case six months and in two cases two and a half to three years. Its appearance was frequently erratic and irregular.

Thirty-five years ago Volhard described physiological albuminuria.

Symptoms in the benign forms of albuminuria are grouped under two main types: (a) the transitory form and (b) the postural form (Isbister). In the transitory form albumin may appear intermittently in the urine, but also in postural albuminuria there are occasional considerable fluctuations. According to Bell, trivial transitory lesions to glomerular capillaries may result in albuminuria, but are so light that they can seldom be found with the microscope. Leube and McLean found "physiological" albuminuria in 5·32% out of 20,000 students in Minnesota. Theobald found albuminuria in 16% of girls aged thirteen to fourteen years, and in 8·2% of women aged over twenty-five years.

In only two out of our 104 cases, slight albuminuria is constantly present and has lasted now for a considerable period. Initially stronger, lately gradually diminishing, it is in one case, that of the patient C., still attended by other signs of kidney damage—namely, disturbances in concentration and dilution, which are irregular, and higher than normal blood urea figures and impaired clearance. This patient was treated for only nine days with lithium and responded with symptoms of moderate toxicity, depression, anorexia and feebleness. The other patient, B., was treated with lithium for three and a half months, and albuminuria was first detected several months after cessation of lithium treatment. The long span between treatment and appearance of albumin in the urine makes the close connexion between cause and effect somewhat doubtful, although the lately dwindling amounts of albumin excreted point to the similarity with the other cases in which lithium produced toxic effects.

On the other hand, spontaneously developing kidney trouble cannot be denied. But such a disorder would produce—especially in the case of C.—a more constant excretion of albumin during a persistent disturbance, however small, of concentration and dilution. Irregularities in concentration and dilution, albuminuria and the absence of occasional erythrocyts and casts do not suggest any common kidney disease. In this connexion it may be said that there could be a resemblance to the initial symptoms caused by other metals and their compounds as mentioned in the introduction, or as caused by other nephrotoxic agents—for example, ether, cantharides, carbon tetrachloride, copaiva, iodine, phenol, turpentine and phosphorus.

With regard to the seven cases of orthotic albuminuria, I again refer to Theobald, who found a trace or more of albumin in the urine of 34% of 110 college girls, in one or more specimens of urine during the day; but in only 10% was albumin detected in the specimens collected immediately after the girls had risen from bed. Salt and McMenemey refer to the high incidence of postural albuminuria. Orthotic albuminuria has become a condition frequently met with, but is no longer regarded as a kidney disease. While it is thought to be a weakness of the kidneys or a type of reaction to pressure, it is conceivable that such kidneys would show lessened resistance to potentially toxic substances like lithium, since an analogy with other metals and their compounds producing distinct kidney damage might be expected. According to our observations, orthotic albuminuria was slightly aggravated by lithium for a limited time.

Slight preexistent albuminuria was also present in two patients aged over thirty-five years, in two patients aged over sixty years and in one patient aged nearly eighty years; but this has not progressed in spite of lithium treatment lasting for several months and two years respectively. This again shows the individual susceptibility to lithium, which appears to be only conditionally nephrotoxic, depending on sodium metabolism or on congenital peculiarities of structure of the kidney. It is only logical to conclude that if lithium was harmful to every kidney under any circumstances, these patients with preexistent albuminuria would have been the first to feel the effect.

It is puzzling that albuminuria can occur some time after cessation of lithium treatment. Chemical affinity can hardly be used as explanation for such a belated action in the kidney unless accumulation and retention of lithium in the body last for longer than four weeks. However, the thought is comforting that all but two cases of albuminuria of those caused by lithium according to our observations were very slight, not coexistent with other kidney symptoms, and disappeared without leaving a trace. In the light of such findings, albuminuria during or after lithium treatment is insignificant and becomes more a clinical interest than a threat of kidney disease.

The conclusion is that the possibility of acquiring a slight kidney complaint is small, though admittedly not entirely out of the question. This should not deter anyone from starting a patient on lithium treatment when it is needed. It has to be borne in mind that occasionally any treatment for psychotic excitement is accompanied by certain risks. But continuation of a manic state for a long period presents a risk in itself. Physically healthy manic patients can gain comparatively more by being freed from their restlessness, excitement, sleeplessness and fury than they can lose by a slight derangement of the kidneys without clinical after-effects, which in 90% of the cases will disappear without leaving a mark behind. The age-old principle "*primum non nocere*" retains its meaning for all physical and mental ailments. I am prepared to gain for manic patients tranquillity and peace of mind at the cost of a minute transitory kidney lesion.

Recent experience has proved the comparative safety of lithium when used together with a sodium-rich diet, which may avert kidney lesions as well as general and gastrotoxic poisoning.

Treatment of Toxic Manifestations.

It is of paramount importance to give protection against possible lithium poisoning by supplementing the diet with additional doses of sodium chloride.

The mention of the very good effect of "Cylotropin" may sound miraculous and astonishing. However, my experience of the result produced by "Cylotropin" in encephalitis goes back to 1925. Several patients treated by 20 cubic centimetres given intravenously recovered very well, a pronounced improvement being noticeable on the second day of treatment. Although this form of treatment was afterwards tried by others with good results, this treatment fell into oblivion owing to the subsequent lack of cases of encephalitis. It is also effective against herpes of virus origin.

It well may be that those cases of viral encephalitis in which "Cylotropin" was tried and proved to be efficient were caused by a virus strain which succumbed to the influence of "Cylotropin", while other strains may be resistant to it. Nevertheless, "Cylotropin" was efficient in these three cases of ours mentioned earlier and it may be worth a trial also in encephalitis of the Australian type.

"Cylotropin" contains 40% hexamethylenetetramine, 16% sodium salicylate, and 1% caffeine. Its pharmacological action consists in releasing formaldehyde from hexamine in an acid urine and it acts in kidney and bladder, but according to my observation also in the bile ducts, gall-bladder and brain.

Though morally bound to use antibiotics in the first place, one occasionally comes across their inefficiency and has to revert to other kinds of treatment. In such cases (especially if the disease is of virus origin, or if its site is in the kidneys), "Cylotropin" may be found very helpful. It can be even combined with antibiotics if they are administered alternately at reasonable intervals. Small doses, five cubic centimetres daily, are inefficient unless administered daily for a long period. Its efficiency is increased and intensified by intramuscular administration of one or two cubic centimetres of an organic iodine preparation (for instance, "Entodon") twelve to twenty-four hours after "Cylotropin" every third or fourth day. "Cylotropin" begins to take effect when the dosage given has reached 10 cubic centimetres. Only a few patients react to hexamine with bladder spasms and stranguria. This can be remedied by calcium given orally and by injection. Sodium thiosulphate, in view of its outstanding action against poisoning by metallic agents, could be another useful drug.

BAL should also be remembered in cases of lithium poisoning.

Summary.

A report on 104 cases of psychotic excitement treated by lithium citrate is presented.

Of the patients 45·19% responded extremely well, 27·88% responded well, and 26·93% failed to respond to treatment. Of this last group 10·58% developed toxic symptoms referable either to the digestive organs or to the nervous system. One patient died from encephalopathy.

If eight patients with orthotic albuminuria are discounted, slight, transitory, innocuous albuminuria was found in 15 cases. The albuminuria lasted for a limited time during or after the conclusion of the treatment and disappeared without leaving a trace. No other symptoms pertaining to any real kidney damage were noticed.

All these cases of albuminuria answer to the description of the group of transient, innocuous, insignificant albuminurias described by Bell, by Theobald, by Isbister, by Allen, by Bing, by King *et alii*, by Salt *et alii*, by Smith, by Volhard and by many others. Only two patients retained gradually diminishing faint albuminuria in conjunction with an irregularity in the concentrating and diluting ability of the kidneys. This may well have developed independently of lithium and from other causes.

The high incidence of toxicity was partly due to selection of unsuitable cases at the beginning of the treatment more than three years ago, and partly due to a low sodium content of the patients' diet.

It is now established that lithium replaces sodium in the body. Its toxicity is reduced by a surplus of sodium in the diet. A rich sodium content in the body guards against the development of toxic symptoms due to lithium, which also can be prevented by strict supervision of the patient.

"Cylotropin" has been used with very good effect in high doses, 10 to 15 cubic centimetres and even 20 cubic centimetres given intravenously or intramuscularly daily for several days in succession in the encephalotoxic cases. The use of sodium thiosulphate, efficient in metallic poisoning, or of BAL should be suitable here.

Contraindications for treatment by lithium are as follows: abnormal quietness, states of depression, agitated melancholia, melancholia, nephritis, albuminuria and intercurrent diseases.

Properly administered, lithium can be regarded as a valuable, useful drug for treatment in mental institutions and even for treatment of selected patients at home.

Cade's introduction of lithium signifies an important and welcome contribution to the armamentarium of treatment for psychotic excitement. It represents a step forward towards the ideal treatment; it is a sedative without narcotic side-effects, without the excessive inconvenience caused to patients and staff by electroconvulsive therapy, it is easy and safe to administer, and it is usable for a fairly long period.

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GAIN IN WEIGHT AND LENGTH IN THE FIRST YEAR OF LIFE OF CHINESE INFANTS BORN IN SINGAPORE IN 1951.

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SOMATIC measurements are often used for the assessment of nutritional status and are most useful when large numbers of people are surveyed. Such methods have their limitations when based upon single estimations; nevertheless, in children the changes in height and weight in relation to age indicate whether growth is proceeding at a satisfactory rate. It is usual to compare the progress of a particular child with that of an "average" child, but the difficulty arises in the selection of the "standard" child. In many countries the standard curves are obtained by plotting the means of the measurements of children who have no obvious physical defects or pathological conditions. In the application of the curve to assess the progress of a particular child it is necessary to determine the range of variation found within the group of apparently normal children. The purpose of this study is to establish growth curves for the first year of life for Chinese infants born in Singapore.

The Selection of the Study Group.

A number of factors were taken into account, and the inclusion of an infant in the study group required the fulfilment of certain criteria.

1. Both parents had to be of pure Chinese ancestry; but no differentiation was made with regard either to the length of sojourn in Singapore or to the province of China from which the parents originated.

2. The infants were born to women who had been admitted to the third-class wards of the Kandang Kerbau Maternity Hospital, Singapore, where they received free medical and hospital attention both before and after confinement. They were drawn from the lower income sections of the community and there was a predominance of the semi-skilled and unskilled trades in the occupations of the fathers at the time of the births of the children. The year 1951 was one of economic stability in Singapore, with relatively little unemployment, and although the cost of living was high compared with the pre-war conditions, wages were adjusted during the year to compensate for this rise.

3. Only single births were considered, and all the infants were classified as "full-term and normal" by the medical staff of the hospital. An infant was excluded from the sample if the history of the mother revealed any abnormalities during pregnancy or delivery.

4. It was decided that the best way to obtain accurate and complete records would be to undertake a series of regular home visits. Problems of staff and transport resulted in the restriction of the study to the urban area of Singapore.

All infants (73 males and 55 females) who fulfilled these requirements between February 5, 1951, and March 30, 1951, were included in the study.

The mothers were interviewed on their discharge from the hospital and were asked if the investigators might visit the home to weigh the baby, but the reason for the inquiry was not explained. Only one household had to be eliminated from the original selection because of lack of cooperation. During the year two infants died, one at six weeks with convulsions, and the other at ten months from gastro-enteritis followed by bronchopneumonia. Twenty-three households moved into areas which were inaccessible; but a total of 103 babies were still under observation until their first birthday.

Tables I and II have been included to compare the selected group with all the "normal, full-term" Chinese infants born in the third-class wards in the hospital in 1951. The age of the mother refers to the age she attained on her last birthday, and the parity includes all previous pregnancies, whether they resulted in live births, still-births or recognized abortions. The birth weight of the baby is the weight measured to the nearest ounce by the hospital staff in the labour ward within a few minutes of birth. It can be seen from Table II that the mean birth weight of the sample is slightly greater than that of the corresponding hospital population for the year. This difference is not significant, and with regard to birth weight the sample is not unrepresentative of the whole.

Methods.

All weighings subsequent to the birth weight determination were performed by the members of the Division of Applied Nutrition, University of Malaya, in the baby's home, usually between 9.30 and 11.30 a.m., and the same balance was used throughout the year. The baby was weighed naked to the nearest half-ounce on the wicker pan of an infant beam type of balance ("The Cromwell House Baby Scale"). Records were kept at fortnightly intervals from birth for the first twelve weeks and thereafter at four-weekly intervals until the age of one year (2055 observations).

Vickers and Stuart (1943) have shown that measurement of length with the baby recumbent is preferable to erect measurement because postural alterations are eliminated; therefore this method was chosen. The birth length was measured by the hospital staff, but all other length measurements were determined by the investigators with the aid of a specially constructed horizontal measuring table (Figure I). The table was made of wood with a board fixed perpendicularly at one end. A second perpendicular board could be moved by being slid along a metal groove inserted down the length of the table. The distance between the fixed and movable boards could be measured on the scale marked near the groove. One investigator placed the naked child on its back on the table and the legs were fully extended by pressing at the knee joints with one hand and holding the ankles firmly with the other hand, so that the soles of the feet were flat against the fixed end. A second investigator held the head by the temples, so that the child was looking upwards, and then adjusted the movable end until it was just in contact with the crown of the head. The length was recorded at 0, 24 and 52 weeks (337 observations).

The investigators were given instructions that they were not to volunteer any information regarding the care of the baby, and if asked for advice they were to suggest to the mother that she should attend a Government welfare clinic or the out-patient department of the General Hospital, Singapore. Every effort was made to ensure that the intrusion of the investigator into the conduct of the home would be minimal, and that the upbringing of the child would be typical of the stratum of society under study.

TABLE I.

The Age and Parity of Chinese Mothers, Third-Class Patients, 1951.

Age. (Years.)	Sample. Number of Women.	Sample. Percentage of Total.	Hospital. Number of Women.	Hospital. Percentage of Total.	Number of Pregnancies.	Sample. Number of Women.	Sample. Percentage of Total.	Hospital. Number of Women.	Hospital. Percentage of Total.
19 and under ..	11	8·59	788	8·31	1	25	19·53	1916	20·20
20 to 24 ..	41	32·03	3173	33·46	2	24	18·75	1792	18·89
25 to 29	29	22·66	2259	23·82	3	23	17·96	1578	16·64
30 to 34	29	22·66	1613	17·01	4	13	10·16	1266	13·35
35 to 39	17	13·28	1160	12·23	5	18	14·06	946	9·97
40 to 44	1	0·78	440	4·64	6	10	7·81	681	7·18
45 and over ..	0	0	51	0·54	7	8	6·25	471	4·97
Unknown.. ..	—	—	1	—	8	4	3·13	334	3·52
					9	1	0·78	206	2·17
					10 and over	2	1·56	295	3·11
Total	128	100·00	9484	100·01	—	128	99·99	9485	100·00
Mean age ..	—	27·2	—	27·4	Mean parity	3·6	—	3·6	—

Results and Discussion.

Gain in Weight.

The average birth weight of the male infant is significantly larger than that of the female infant (Millis, 1952) and therefore the sexes have been considered separately; Table III sets out the median, tenth and ninetieth centiles of the weight measurements for male and female infants. These levels were obtained by placing the weights of the children in lists in ascending order. The lists were then

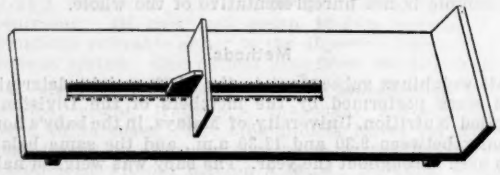

FIGURE I.

The horizontal table used for measurement of length.

divided into 100 equal parts, and the weight of the child occupying the tenth, fiftieth, and ninetieth positions was ascertained for each age group.

In Figure II a comparison is made between the weights obtained in this series and those for infants in other countries. The American figures were obtained by Vickers and Stuart (1943), of the Department of Maternal and Child Health, Harvard School of Public Health in Boston, and are based on repeated measurements at selected age groups of more than 100 male and 100 female white infants. The figures of Clements (1933) for Australian infants were based on approximately 30,000 observations of 602 female and 613 male infants who were considered to be a fair average sample of the community. The Chinese figures were reported by Gin (1948), and were derived from 1212 measurements for male and 674 measurements for female infants.

TABLE II.

The Birth Weights of "Full Term, Normal" Chinese Infants, Third-Class Patients, 1951.

Weight.	Male Infants. Sample: Number.	Male Infants. Hospital: Number.	Female Infants. Sample: Number.	Female Infants. Hospital: Number.
3 lb. 0 oz. to 3 lb. 7 oz.	0	0	0	0
3 lb. 8 oz. to 3 lb. 15 oz.	0	0	0	1
4 lb. 0 oz. to 4 lb. 7 oz.	0	4	0	3
4 lb. 8 oz. to 4 lb. 15 oz.	0	26	0	27
5 lb. 0 oz. to 5 lb. 7 oz.	1	193	2	245
5 lb. 8 oz. to 5 lb. 15 oz.	4	460	7	536
6 lb. 0 oz. to 6 lb. 7 oz.	15	877	12	1066
6 lb. 8 oz. to 6 lb. 15 oz.	20	1143	10	1103
7 lb. 0 oz. to 7 lb. 7 oz.	12	1094	9	865
7 lb. 8 oz. to 7 lb. 15 oz.	14	657	12	425
8 lb. 0 oz. to 8 lb. 7 oz.	6	324	3	204
8 lb. 8 oz. to 8 lb. 15 oz.	0	105	0	50
9 lb. 0 oz. to 9 lb. 7 oz.	1	39	0	21
9 lb. 8 oz. to 9 lb. 15 oz.	0	9	0	2
10 lb. 0 oz. to 10 lb. 7 oz.	0	3	0	2
10 lb. 8 oz. to 10 lb. 15 oz.	0	1	0	0
Total	73	4935	55	4550
Mean birthweight ..	7·03 lb.	6·91 lb.	6·84 lb.	6·71 lb.
Standard deviation ..	0·76	0·86	0·80	0·80

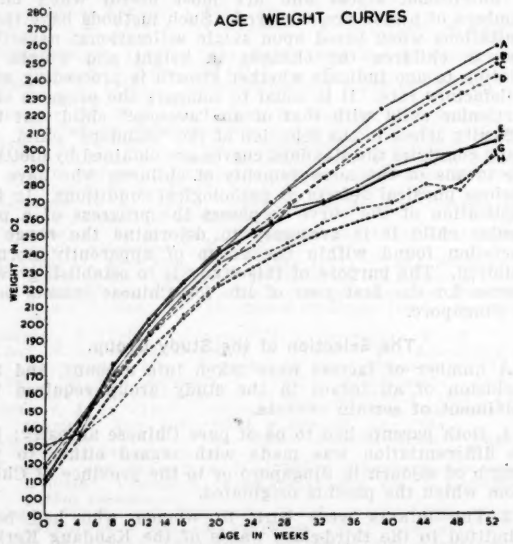

FIGURE II.

The comparison of gain in weight of infants in different countries: A, Caucasian male, America; B, Caucasian male, Australia; C, Caucasian female, America; D, Caucasian female, Australia; E, Chinese male, Peiping; F, Chinese male, Singapore; G, Chinese female, Peiping; H, Chinese female, Singapore.

It can be seen that the curves for Chinese infants in Singapore are similar to those for Chinese infants in China, where there are pronounced seasonal changes, and it could be concluded that differences in climate did not influence the progress of the child in the first year. The weight increases at a similar rate to that of white infants for about twenty weeks, but the Chinese infant makes slower progress in the second six months of the first year. A

similar observation has been recorded for African tribes by Orr and Gilks (1931), by Woodrow and Robertson (1950), and by Jelliffe (1952), and for Negro infants living in America by Dodge (1927).

At the age of one year the average Chinese male infant is 47 to 54 ounces lighter than the corresponding white infant, and the difference between female infants is 54 to 60 ounces in favour of the white child.

TABLE III.

The Weight in Relation to Age of Chinese Infants in Singapore.

Age in Weeks.	Weight in Ounces.					
	Males.			Females.		
	Tenth Centile.	Median.	Ninetieth Centile.	Tenth Centile.	Median.	Ninetieth Centile.
0	96	108	128	92	108	123
2	101	119	139	101	118	132
4	119	142	164	115	132	151
6	133	162	184	127	148	166
8	146	179	203	139	162	182
10	161	193	221	152	175	195
12	171	206	225	160	184	205
16	194	227	251	176	202	229
20	203	244	269	190	216	251
24	219	256	284	200	231	263
28	226	260	290	210	241	276
32	235	267	297	215	247	283
36	247	276	304	225	252	287
40	258	280	310	235	261	296
44	258	287	323	243	267	301
48	266	293	333	248	275	309
52	270	303	337	254	283	319

Increase in Length.

The birth length of 4928 males and 4546 females all of pure Chinese ancestry was measured in the hospital, and the mean length was 19·3 inches for male and 19·0 inches for female infants. The mean lengths of the study group corresponded to that of the hospital population. The increase in length with age of infants in different countries can be compared by the use of Table IV. The progress of Chinese infants in Singapore is similar to that in Peiping.

TABLE IV.

Comparison of Lengths of Different Infants at Various Ages.

Place.	—	Sex.	Length in Inches.		
			At Birth.	Six Months.	Twelve Months.
Singapore ..	Mean.	Male ..	19·3	26·8	28·9
		Female	19·0	26·3	28·6
Peiping ..	Mean.	Male ..	19·6[1]	25·6[2]	28·9[2]
		Female	19·2[1]	25·4[2]	28·1[2]
Boston, U.S.A.	Median.	Male ..	19·9[3]	26·1[3]	29·6[3]
		Female	19·8[3]	25·7[3]	29·2[3]

[1] Tso, 1930.
[2] Guy *et alii*, 1937.
[3] Vickers and Stuart, 1943.

The white American child shows the same increase in length as the Chinese child in the first year; but the average American baby is longer at birth and this advantage is maintained. In all cases the average male is longer than the average female infant.

It is well known that Asians are, on an average, shorter and lighter than Europeans of the same age group (Oliveiro, 1937; Worth, 1947; Burgess, 1948), and it would appear from this study that differences in stature are evident at a very early age.

Summary.

Regular visits were made to the homes of 73 male and 55 female "full-term, normal" Chinese infants of lower income group families; 2055 observations of weight and 337 of length were recorded during the first year and age-weight curves were constructed. The gain in weight of Chinese infants was similar to that of Caucasian infants for the first twenty weeks of life, but after six months of age the increase was noticeably slower.

Acknowledgements.

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A REVIEW OF THE METABOLISM OF POTASSIUM.[1]

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IN 1944 a report of a clinico-pathological conference at the Massachusetts General Hospital (Cabot, case 30451, 1944) described the peculiar gasping respirations just prior to death of a patient suffering from diabetic acidosis who had been treated intensively with insulin, normal saline and glucose. Apparently even the astute clinicians of Boston at that time did not realize that such symptoms might have been due to potassium deficiency, though Aitken (1937) had shown some years earlier that attacks of muscular weakness in familial periodic paralysis were associated with a fall in the level of potassium in the serum.

Jacob Holler (1946) reported the first accurate description of paralysis in diabetic coma that was attributed to potassium deficiency. His patient was dramatically revived by an infusion of potassium after she had spent some hours in a respirator. At about the same time Darrow (1946) produced convincing evidence that severe diarrhœa in infants led to a grave depletion of body potassium and that suitable electrolyte therapy which included potassium greatly improved the prognosis. From this time on

[1] Read at a meeting of the Section of Medicine of the New South Wales Branch of the British Medical Association on July 2, 1953.

the interest of the clinician in potassium metabolism has progressively increased and it has been boosted by the introduction of the flame photometer, which has made chemical estimation of potassium and sodium much more rapid and simple.

Distribution of Potassium in the Body.

The concentration of potassium inside the cells is of the order of 100 milliequivalents per litre of intracellular water, whereas the concentration in the extracellular fluids, including the blood plasma, is about five milliequivalents per litre. In plasma potassium is largely ionized, but within the cell it is combined with protein as an essential ingredient of protoplasm and, together with phosphate, it is combined with glucose and glycogen. Such combinations had been thought to be firm and stable; but work with radioactive potassium has shown that almost all the intracellular potassium of tissues such as the muscles and viscera is continually being exchanged with the general body pool of potassium. The rate of exchange differs in the various tissues of the body.

Though there may be some delay in the passage of ingested potassium across the intestinal epithelium, once it reaches the circulation, after either intestinal absorption or parenteral injection, it diffuses with great rapidity throughout the extracellular fluid. Walker and Wilde (1952) studied the rate of exchange of potassium between plasma and tissues of the rabbit by means of radioactive K^{42}. They found that the fall in plasma concentration after intravenous injection was so rapid that they were unable to draw arterial blood samples into syringes frequently enough to construct an accurate curve. By inserting a length of polyethylene tubing into the carotid artery they were able to show that 90% of the injected potassium passed out of the circulation in one minute. They suggested that this rapid transfer was due to filtration through capillaries throughout the body and was not entirely due to concentration in special viscera. Tissue analyses at the end of two minutes revealed that the visceral organs, comprising only 10% of the body weight and containing about 10% of the total body potassium, now contained 50% of the injected potassium. The highest concentration was found in the kidney.

Corsa *et alii* (1950), also employing radioactive K^{42}, estimated the amount of exchangeable potassium in normal men. They obtained human tissues during operations, or by biopsy, at varying periods after the injection of the test dose. These determinations showed that injected K^{42} was not distributed equally throughout all body potassium within fifty hours. Exchange between tissue potassium and plasma potassium was rapid in the liver, slower in muscle, and slower still in the red cells. The mean amount of total exchangeable potassium in the body was 3400 milliequivalents, and this was approximately proportional to the body weight. They considered that this exchangeable potassium content was 5% less than the total body potassium, the difference being due to the small amount of potassium in red cells, brain and bone that was unexchanged at the end of forty hours after K^{42} administration.

The passage of potassium across the cell membrane and the maintenance of the gradient between intracellular and extracellular potassium both require energy derived from cellular metabolism (Drabkin, 1952). As the red blood cell is the only form of body cell that is readily available for isolated study, it has been used extensively for investigations on energy exchange across the cell membrane. It is postulated that potassium ions which diffuse through the cell membrane are combined promptly with glucose and phosphate to form potassium glucose diphosphate. This salt is poorly ionized, so that the concentration of free potassium ions tends to fall inside the cell and more are able to diffuse through the cell membrane. The combination of potassium, glucose and phosphate requires energy, which is probably derived from the breakdown of adenosine triphosphate, and is dependent on an appropriate enzyme system for the speed of its reaction. The potassium which has entered the cell is later combined more slowly with protein and with glycogen.

Renal Excretion of Potassium.

Normally about 900 milliequivalents of potassium are filtered through the glomeruli each twenty-four hours, and only 75 to 100 milliequivalents are excreted in the urine. Thus 90% or more of the filtered potassium is reabsorbed by the renal tubules. However, it has been shown (Berliner *et alii*, 1950) that secretion of potassium ions by the renal tubules must take place when sufficiently large loads of potassium are administered. This secretory process involves an exchange of potassium ions within the cells of the distal tubule for sodium ions within the lumen of the tubule. Pitts *et alii* (1948) have shown that the acidification of the urine is dependent on the secretion into the tubular lumen of hydrogen ions which are exchanged with sodium ions. This secretion of hydrogen ions cannot take place unless carbonic anhydrase is available to hasten the production of bicarbonate from carbon dioxide. Berliner *et alii* (1951) investigated the effect of a new sulphonamide compound, 6063, on the renal output of hydrogen and potassium ions in the dog. This drug is a powerful inhibitor of carbonic anhydrase, and in these experiments it was found to abolish any evidence of acidification of the urine and invariably to increase potassium excretion. The authors deduced that there is competition between hydrogen and potassium ions for some component of the ion exchange mechanism whereby sodium is reabsorbed in the distal tubule. With alkalosis of the body fluids the cells involved in the ion exchange mechanism would tend to exchange potassium, rather than hydrogen, for sodium. Thus excess potassium would be excreted. In acidosis one would expect hydrogen ion secretion to take place at the expense of potassium, and retention of potassium would occur. . When the concentration of potassium in the body fluids is low, then hydrogen ions rather than potassium ions would be exchanged for sodium, and an acid urine would be produced, even though alkalosis was present in the extracellular fluids.

It seems certain that this correlation with hydrogen ion secretion is only one of the factors that influence the output of potassium by the kidney. In some states of acidosis, such as diabetic coma, potassium excretion is high and the urine is very acid. In such cases potassium is excreted in the urine in combination with the excess acidic radicles.

The urinary output of potassium is influenced, too, by the adrenal cortical steroids. When the supply of cortical hormone is low, as in Addison's disease, there are a diminished output of potassium and an increased output of sodium. When excessive amounts of adrenal steroids are circulated to the kidney in Cushing's syndrome, in stress states or in the course of therapy with adrenocorticotrophic hormone, cortisone or desoxycorticosterone, the excretion of potassium is usually increased and the excretion of sodium is usually diminished.

When a dose of potassium is given to a normal animal it is excreted more or less quantitatively in the urine. Of course, the actual molecules of the administered dose are freely interchanged with the greater part of the total potassium in the body, but there is no appreciable retention after equilibrium has been attained. When the intake of potassium is sharply reduced or abolished—for example, during starvation or during parenteral feeding with potassium-free fluids—the renal output of potassium continues for some days at a relatively high level. On the other hand, when the intake of sodium is similarly reduced the quantity of sodium excreted in the urine promptly falls to a very low level. The potassium that is excreted during starvation comes from the cells, partly from the metabolic breakdown of protein, partly from the breakdown of other compounds of potassium with phosphate and carbohydrate. The potassium set free from combination with protein is excreted in the urine in the ratio of about 2·8 milliequivalents of potassium per gramme of nitrogen.

Careful balance studies on normal individuals have recently been reported. Black (Black and Milne, 1952; Black, 1953) used a diet of glucose and milk from which potassium had been largely removed by a cation exchange resin. Fourman and Ainley-Walker (1952) ingested a

cation exchange resin with a normal diet. In both groups of experiments the caloric intake was sufficient to prevent undue catabolism of protein, so that the large deficits of potassium that were produced were derived from cellular constituents other than protein. These deficits, at least in the experiments of Black and Milne, were due to continued high urinary excretion of potassium during the first few days, in spite of a moderate fall in the level of serum potassium. By the sixth day the output of potassium fell greatly owing to more effective renal conservation of this ion. In most clinical disorders associated with a low intake of potassium this renal conservation is seldom seen, as tissue protein is usually rapidly broken down because of starvation, fever or the hypersecretion of adrenal cortical steroids.

When potassium is administered to an animal whose tissues have been previously depleted of potassium it is retained until the requirements of the tissues have been satisfied. Once the stores are replete any excess potassium that is given is almost quantitatively excreted in the urine. The total amount of potassium that is retained during the treatment of potassium deficiency is assumed to be equal to the amount lost during the development of the deficiency. That this assumption is probably true has been confirmed by studies with radioactive K^{42}, in which the increase in exchangeable body potassium after therapy was found to be almost identical with the observed total cumulative retention (Schwartz and Relman, 1953).

In renal disease retention of potassium is more common than excessive loss. However, it is remarkable how infrequently hyperpotassæmia is seen in chronic renal disease progressing to uræmia. Adequate excretion of potassium is maintained even when the glomerular filtration rate has fallen very low. When renal function ceases abruptly—for example, in surgical anuria or lower nephron nephrosis—the concentration of potassium in the extracellular fluids increases steadily until it causes death by its toxic action on the heart. Potassium may be lost in excess through the kidneys in some types of renal disorder in which the tubular mechanisms for dealing with potassium are affected, and depletion of the body stores may occur in spite of a normal intake in the diet. Such a case has been described by Earle *et alii* (1951).

Hunter and Read (1953) have reported the instructive history of a woman who developed anuria following hæmorrhagic shock. The concentration of potassium in her serum rose to 8·5 milliequivalents per litre within forty-eight hours at the same time as the electrocardiographic tracing showed gross changes of potassium intoxication. The hyperpotassæmia receded with treatment. Profuse diuresis began about the twelfth day and eliminated so much potassium that she began to suffer from symptoms of hypopotassæmia by the fifteenth day. Under such conditions the newly functioning tubular epithelium has difficulty in reabsorbing not only potassium but also the other filtered electrolytes, so that disproportionate renal losses of sodium, chloride and calcium may also be expected.

Relation of Potassium to Neuro-muscular Function.

The symptoms of potassium deficiency or potassium excess are almost entirely due to disturbance of function of muscle or nerve. The subject is a complex one and our knowledge is fragmentary, though it has received attention from physiologists since the days of Ringer's perfusion experiments on the isolated heart. An excellent review by Botelhoe and Comroe (1952) has summarized most of the known facts.

According to the theory of Nachmansohn (1948), the passage of an impulse along a nerve fibre involves the transfer of potassium ions through the outer membrane of the nerve to the extracellular fluids, and a movement back again of the potassium ions when the nerve is repolarized. Acetylcholine is said to facilitate the transfer by lowering membrane permeability. A similar mechanism involving a shift of potassium ions through the cell membrane probably occurs during the transmission of an electrical impulse through cardiac muscle. Though the exact mode of conduction through nerve fibres is debated, there is no doubt that either too low or too high a concentration of potassium in the fluid around a nerve will depress conductivity, perhaps by altering the gradient of potassium concentration between the intracellular and extracellular fluids.

Transmission of an impulse across the neuro-muscular junction is dependent on the activity of acetylcholine. This is synthesized rapidly, where needed, by the enzyme choline acetylase, and destroyed again rapidly by choline esterase. The chemical interaction, which is facilitated by choline acetylase, between acetylphosphate and choline to form acetylcholine requires the presence of potassium ions. Thus when potassium is insufficient, the production of acetylcholine may be impaired and neuro-muscular transmission may be blocked.

It should be pointed out at this juncture that acetylcholine is involved also in the activity of autonomic ganglia and in the secretion of the digestive enzymes by the intestinal glands. Lack of potassium may impair the functional activity of these structures in a similar fashion.

Though alteration in the concentration of potassium at the neuro-muscular junction may cause muscular weakness, there is no doubt that potassium exerts a direct effect on the muscle fibre itself. Green *et alii* (1952) showed that there was a rapid decline in the amplitude of contraction of the isolated papillary muscle of the cat when the concentration of potassium in the surrounding medium was too high or too low. It would seem apparent that an optimum concentration of potassium both within the muscle cell and in the surrounding fluid is essential for the functions of contractility, excitability and rhythmicity to be efficiently carried out. Paralysis has been noted (Finch *et alii*, 1946) in association with both very low and very high levels of potassium in the plasma.

Clinically, however, is the concentration of potassium in the extracellular fluids or in the cell the more important in producing symptoms?

When potassium is retained in excess in the body there is little doubt that it is the increasing level in the extracellular fluids, as reflected in the plasma, that produces the deleterious effects. There is no proof that high concentrations of intracellular potassium are harmful; but high concentrations in the extracellular fluid can rapidly cause death from cardiac standstill or ventricular fibrillation long before any appreciable intracellular transfer could take place.

When symptoms are due to deficiency of potassium it has been usually assumed that the low level in the extracellular fluid is more important than the diminution in intracellular content and concentration. It is very probable that both factors play a part in producing the clinical syndrome, but there is some evidence that muscular paralysis can occur in states of potassium depletion, even though the serum potassium level remains normal or even high.

Streeten and Vaughan Williams (1952) carried out experiments on dogs to determine the influence of electrolytes on intestinal motility and tone. Depletion of sodium and chloride was produced by intraperitoneal injections. Paralytic ileus developed in association with a large rise in plasma potassium and a presumed fall in intracellular potassium. They stated that the depression of intestinal propulsion was consistent with the hypothesis that it was primarily due to loss of cell potassium. Again, it is stated (Streeten and Ward-McQuaid, 1952) that recent evidence is consistent with the view that intracellular, though not extracellular, potassium deficiency can cause paralysis of intestinal motility both *in vivo* and *in vitro*. The hypothesis is interesting, but the evidence is not conclusive and is open to other interpretations.

Denton *et alii* (1951) described electrocardiographic changes typical of hypopotassæmia at a time when the plasma potassium level was 7·5 milliequivalents per litre. Henderson (1953) has also reported electrocardiographic changes in diabetic acidosis that were poorly correlated with the concentration of potassium in the serum. Black (1953) showed that in pure, uncomplicated potassium depletion the level of potassium in the plasma fell roughly

in proportion to the total body deficit. When, as is frequently seen in clinical practice, the loss of potassium is accompanied by undue losses of sodium and water, the shrinkage in the volume of the extracellular fluid may cause the concentration of potassium in the plasma to remain high despite extreme intracellular deficits. At this stage it may be difficult to make the diagnosis of intracellular depletion, except by deduction from the history, until the extracellular space has been reexpanded by administration of fluids containing sodium and chloride. Once the extracellular volume has been restored the level of potassium in the plasma tends to fall, partly through simple dilution, partly through increased excretion by the kidneys.

In periodic familial muscular paralysis the attacks are usually related to a fall in the level of potassium in the serum, though typical cases have been described (Tyler *et alii*, 1951) in which no correlation of the attacks with the serum potassium concentrations could be established. The fall of serum potassium content that precedes the usual attack is not due to any increase in excretion and is apparently due to transfer of potassium from the extracellular fluid to within the cells. This transfer is accelerated by procedures that increase the binding of potassium with carbohydrate, so that attacks may be precipitated by administration of glucose or insulin. It would appear that in this disorder the muscular paralysis is definitely due to a fall in extracellular rather than in intracellular potassium concentration. However, I do not think the possibility can be excluded that abnormal binding of potassium with glucose and phosphorus may lower the concentration of available ionic potassium within the cell, in spite of an increase in the total amount of intracellular potassium.

Influence of Potassium on Cerebral Function.

Insufficient attention has been paid in the past to the effect of disturbances of potassium metabolism on the brain. At least one instance of acute confusional psychosis developing during the course of treatment with ACTH and associated with a low level of serum potassium has been described (Ransohoff *et alii*, 1951). The psychosis was promptly relieved by administration of potassium. The patient, mentioned above, who developed hypopotassæmia after an acute anuric episode became psychotic, but improved when the level of serum potassium was raised. In their description of the post-operative state associated with a deficit of potassium, Eliel *et alii* (1950) referred to the apathy and lethargy that these patients exhibited, and commented on the prompt improvement in mental attitude that followed administration of potassium chloride. Similar observations have been made by resident medical officers at the Royal Prince Alfred Hospital who have been observing such patients closely. It is, of course, frequently difficult to distinguish the effects of potassium deficiency from other associated disturbances that may influence cerebral activity, such as alkalosis, acidosis, starvation or lack of vitamins.

Metabolic Alkalosis in Potassium Deficiency.

Alkalosis as a result of potassium deficiency has been noted in a variety of clinical disorders. The high plasma bicarbonate level is associated with a low plasma chloride concentration, and it cannot be reduced by administration of saline or ammonium chloride unless potassium is also given. Although the alkalosis is most pronounced when potassium deficiency is accompanied by vomiting with loss of chloride in the gastric juice, it can occur when no such loss of chloride has taken place.

Darrow (1950) has discussed fully the production of alkalosis due to potassium deficiency in rats and men. He has stressed the point that alterations in the acid-base equilibrium of the extracellular fluids can influence intracellular composition, and that alterations in intracellular composition can influence the ionic pattern of the extracellular fluids. These are biological equilibria that require adequate renal adjustment. Black (1953) showed that a rise in serum bicarbonate content followed pure dietary deficiency of potassium, and he discussed at some length the theories of production of this phenomenon.

At present I think it can be said that the exact mechanism by which potassium deficiency produces alkalosis is by no means certain. The process described by Berliner *et alii* (1951), by which potassium lack impairs the ability of the kidney to secrete alkaline urine, may play some part. During potassium depletion sodium enters the cells to replace about two-thirds of the lost potassium. Cooke *et alii* (1952) suggested that hydrogen ions entered the cells from the extracellular fluid to make good the deficit of cations within the cell, thus leaving an extracellular alkalosis.

From the practical viewpoint, the demonstration of a high plasma bicarbonate level and a low plasma chloride level in a patient suspected of suffering from potassium deficiency would help to confirm that diagnosis, perhaps when facilities for potassium estimations were not available and electrocardiographic changes were absent or equivocal. If in such a patient the alkalosis did not respond to judicious treatment with saline and ammonium chloride, the diagnosis of potassium lack would be clinched.

Potassium Metabolism in Diabetic Acidosis.

Though a large cellular deficit of potassium is invariably found in severe diabetic acidosis, and a fall in the level of plasma potassium during treatment is the rule, clinical manifestations of potassium lack are not very common. Root (1952) has said in reference to diabetic acidosis, "we have not yet seen clinical hypokalemia developing during the course of treatment". However, there is no doubt that deaths from cardiac or respiratory paralysis can occur in diabetic coma from potassium deficiency, and that such deaths should be preventible.

In considering this problem it is important to distinguish clearly between the metabolic changes that take place during the development of the ketosis and the changes after treatment with insulin and saline has begun. The following factors contribute to potassium depletion in patients with uncontrolled diabetes progressing to coma.

1. Owing to lack of insulin, breakdown of glycogen is greater than its synthesis. The potassium combined with glycogen is liberated inside the cell and diffuses out into the extracellular fluid. The other intracellular carbohydrate potassium compounds also are broken down.

2. Protein in the cells is catabolized, particularly in the liver, because of the unregulated gluconeogenesis. The catabolic action of the adrenal cortical steroids, secreted in response to the stressing stimulus, also contributes to protein breakdown and nitrogen loss. Potassium set free from combination with protein is excreted in the urine in constant proportion to nitrogen, so long as kidney function remains adequate.

3. The osmotic diuresis caused by high concentrations of glucose in the renal tubules washes out electrolytes, including potassium.

4. As the rate of production of ketonic acids increases, potassium, with other basic radicles, is excreted in the urine in increasing amounts in combination with these acids.

5. Dehydration, leading to contraction of the extracellular space, is a sequel to the diuresis and electrolyte loss. Water leaves the cells to aid in maintaining the volume of the extracellular fluid, and potassium passes out with the water. Seldin and Tarail (1950) have shown that the high glucose content of the extracellular fluid increases the loss of intracellular water and potassium by its osmotic activity, since glucose passes only slowly through the cell membrane.

6. Food intake is frequently negligible during the state of ketosis, and vomiting often aggravates fluid and electrolyte loss.

These multiple factors contribute towards a total deficit of body potassium, almost all of which comes from inside the cells. The concentration of potassium in the extracellular fluids, including the plasma, at this stage is usually normal or high, as potassium is continually passing into

the extracellular fluid from the cells and the volume of the extracellular space is greatly shrunken.

When treatment is commenced almost all these processes are reversed. The rate of loss of potassium from the body rapidly diminishes, but nevertheless the concentration of potassium in the extracellular fluid falls. This is brought about by two mechanisms. Firstly, potassium reenters the cells as cellular dehydration is overcome and glycogen is reformed; secondly, administration of saline solution expands the extracellular space and dilutes the potassium remaining there.

With these points in view it would seem that the following principles should be followed.

1. Potassium therapy at the beginning of treatment of diabetic coma is dangerous and unnecessary. Initial treatment should be given with fluids similar in composition to the extracellular fluid.

2. Therapy designed to replenish the intracellular electrolytes with fluids including potassium, and probably also magnesium and phosphate, may well be commenced when the dehydration has been partly overcome and the blood sugar level is beginning to fall. Such therapy would usually be safe after the fourth hour of treatment, even without the aid of the flame photometer to estimate the level of plasma potassium.

3. If it is possible to give potassium salts, or fluids such as orange juice, broth, or milk by mouth, then this method should be preferred to parenteral infusions.

4. When urinary output is inadequate, solutions containing potassium should be given with great caution, and then only when accurate biochemical and electrocardiographic control is available.

Potassium Deficiency in Gastro-Intestinal Disorders and Post-operative States.

Loss of potassium due to vomiting, gastric suction, discharge from intestinal fistulæ or diarrhœa is by far the commonest type of clinical potassium deficiency. Other important contributing factors in causing potassium depletion in surgical patients are prolonged, and sometimes excessive, saline therapy, and adrenal cortical hyperactivity from the stress of operation. The vital importance of replacing tissue potassium deficiencies in cases of infantile diarrhœa was first pointed out by Darrow (1946), and it has been recently emphasized by Howard Williams (1952).

A characteristic post-operative syndrome of potassium depletion was described clearly by Eliel *et alii* (1950). In his recent Hunterian Lecture, Starr (1953) drew attention to the role of potassium deficiency in causing acute dilatation of the stomach, and emphasized the magnitude and significance of the circulation of electrolytes in the gut.

Influence on Cardio-vascular Function.

The effect of excess or deficiency of potassium on the heart has been touched on previously. The subject has received much attention in the literature and needs little elaboration here. Low levels of potassium in the plasma and in the cardiac muscle cells impair cardiac function and cause typical changes in the electrocardiogram of depressed *S-T* intervals, prolonged *Q-T* intervals, and lowered *T* waves. High levels of potassium in the plasma are more toxic to the heart and may lead to sudden death. The first changes in the electrocardiogram due to hyperpotassæmia are "tenting" and increased height of the *T* waves; later the *P* waves recede and bizarre ventricular complexes appear.

There is evidence (Perkins *et alii*, 1950) that severe prolonged potassium deficiency can damage the muscle fibres of the heart and produce necrosis and fibrosis in the myocardium.

Treatment of Potassium Deficiency.

Without going into details regarding potassium administration, I wish to emphasize some important points.

1. Oral administration of foods rich in potassium, or of appropriate salts of potassium, is always to be preferred to parenteral infusion if it is practical.

2. Repair of any extracellular deficit with adequate salt and water should precede potassium therapy.

3. The danger of giving potassium is entirely due to the toxic effect on the heart of a high concentration of potassium in the blood reaching the heart. When given by intravenous injection the solution reaches the heart before it has had opportunity to diffuse through the other body tissues. Intraarterial infusions of potassium solutions can be given to animals at a considerably higher rate than can intravenous infusions, as some of the potassium diffuses through the capillaries before returning to the heart (Fenn, 1940). In states of potassium depletion a total cellular deficit of several hundred milliequivalents is common, so that a rise in the general level of extracellular potassium is not a very serious danger if even large amounts of potassium are administered slowly. Hence it is recommended that intravenous infusions of potassium should seldom be given at a rate greater than 10 milliequivalents per hour. This corresponds to giving a litre of Darrow's solution in three to four hours.

4. If renal function is defective, the risk of producing an excessive rise in extracellular potassium is much greater. Every effort should be made to promote and maintain an adequate urinary flow by salt and water replacement prior to potassium administration. In certain cases potassium treatment may be obligatory in spite of defective renal function, but great caution should be observed.

5. With these precautions in mind, it is logical to recommend that replacement of deficits of intracellular electrolytes, particularly potassium, should be made in those cases in which the clinical picture, corroborated where possible by laboratory aids, indicates that large losses of these elements have occurred.

Conclusion.

Throughout this discussion emphasis has been concentrated on one single electrolyte. It would be quite wrong to convey the impression that this represents a balanced over-all picture of electrolyte disturbances in general. Upsets of sodium and chloride balance are far more common and important, and their significance is more widely appreciated. Disorders of electrolyte balance must be viewed against the background of the total ionic pattern of the body.

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Reviews.

Endocrinology in Clinical Practice. Edited by Gilbert S. Gordan, M.D., Ph.D., and H. Lisser, M.D.; 1953. Chicago: The Year Book Publishers, Incorporated. 9" x 6¼", pp. 416, with 90 illustrations, three in colour. Price: $10.50.

THIS volume is based on a series of lectures on clinical endocrinology and metabolic diseases presented in 1952 by the University of California School of Medicine. The great majority of the authors are members of the staff of this university and represent a wide range of scientific and clinical experience. The practical approach of the contributors towards their subject is foreshadowed by the opening sentence in the book, in which the senior editor, H. Lisser, a veteran of thirty-five years on the endocrine battlefront, makes the following statement: "In no other branch of clinical medicine is the information provided by a detailed history and a thorough physical examination more rewarding than in the field of endocrine disorders."

The essays generally maintain a very high standard and deal with a wide field of clinical endocrinology. They are deliberately simple and dogmatic, with little discussion of controversial pros and cons and few references to the literature. They are the considered opinions of experienced clinicians on the diagnosis and management of the disorders they discuss. The chapter on the thyroid gland contains a great deal of concise and up-to-date information compressed into 37 pages. A section on progressive exophthalmos by H. C. Naffziger is of particular interest. The parathyroid glands and metabolic bone diseases are adequately discussed in line with the teachings of Fuller Albright. The account of the pituitary gland is succinct and practical and includes a section on *anorexia nervosa* by L. S. Craig, in which the distinction of this malady from pituitary insufficiency is carefully described and illustrated by apposite case reports. P. H. Forsham writes with authority on the adrenals and devotes a section to the use of corticotrophin and cortisone in general therapy. The chapter on carbohydrate metabolism and diabetes suffers from undue compression, and some statements might be misleading if they were accepted uncritically—for example, the suggestion that intravenous fluid replacement may be unnecessary in the treatment of elderly patients suffering from diabetic coma, or the advice that a safe dose of insulin for a child may be estimated on the basis that one unit of insulin will metabolize about two grammes of body glucose. The chapter on the male and female gonads is very good. Many aspects of this complex field are reviewed pithily and clearly, and the recommendations for therapy are based on a firm physiological foundation.

This book can be warmly recommended as an excellent series of studies in endocrinology. It is not a book for the research worker or the specialist in endocrine disorders, but is particularly suitable for the informed general practitioner, the general physician or the general surgeon who wishes to bring his knowledge in this field up to date.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"The Heart Beat: Graphic Methods in the Study of the Cardiac Patient", by Aldo A. Luisada, M.D.; 1953. London: H. K. Lewis and Company, Limited. 10" x 7½", pp. 540, with *273 illustrations. Price: 84s.*

Written to correlate a great mass of data on graphic methods, to present them with a unified concept and to correlate them with the appropriate clinical pictures.

"A Handbook for Dissectors", by J. C. Boileau Grant and H. A. Cates; Fourth Edition; 1953. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. *7½" x 5", pp. 440, with 26 text figures. Price: £1 17s. 9d.*

In this edition the thorax "has received special attention".

"Supplement to the S.F.A. Catalogue of Medical Films"; 1953. London: Harvey and Blythe, Limited. 8½" x 5½", pp. 60. Price: 6s.

This is a supplement to the Catalogue that was published in 1952.

"Pathology", edited by W. A. D. Anderson, M.A., M.D., F.A.C.P.; Second Edition; 1953. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical), Limited. 10" x 7", pp. 1408, with 1251 illustrations, 10 in colour. Price: £8 8s.

Intended for all students of pathology; for the beginner the larger type is intended to suffice.

"Shock and Circulatory Homeostasis: Transactions of the *Second Conference, October 19, 20 and 21, 1952, Princeton, N.J.*", edited by Harold D. Green, M.D.; 1953. New York: Josiah Macy Junior Foundation. 9" x 6½", pp. 276, with 57 text figures. Price: $3.75.

The contents deal with "Metabolic Aspects of Hæmorrhage and Traumatic Shock" and "Distribution and Possible Physiologic Functions of Epinephrine and Nor-Epinephrine".

"The ABC of Motherhood", by Clair Isbister, M.R.A.C.P., D.C.H. (London). Sydney: Australian Broadcasting Commission. 5½" x 4", pp. 32, with about 12 text figures. Price: 1s.

The four talks are: "Are You Preparing for a New Baby in Your House?", "Preparation for Childbirth", "What You Will Need for Baby" and "After Baby Comes Home".

"May's Manual of the Diseases of the Eye: For Students and General Practitioners", revised and edited by Charles A. Perera, M.D.; Twenty-First Edition; 1953. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 8" x 5½", pp. 520, with 378 illustrations, 93 in colour. Price: £3 4s. 6d.

The first edition was published in 1900.

The Medical Journal of Australia

SATURDAY, FEBRUARY 20, 1954.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given without abbreviation: surname of author, initials of author, year, full title of article, name of journal without abbreviation, volume, number of first page of the article. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

THE FEDERAL COUNCIL MEDICAL MONOGRAPH FUND.

TIME and time again during the last few years the view has been expressed in this journal that the results of medical research carried out in Australia should, if possible, be published in Australia. It has been stated that Australia is old enough to stand on her own legs in this regard, and few will venture to deny the truth of this statement. Research workers in this country are probably torn between two desires. On the one hand, they wish probably to have their work put before the largest possible audience and they know that this audience exists in Great Britain and in America. On the other hand, they realize that Australian work, though it is of benefit to the world at large, does reflect credit on Australian centres of research, and they naturally wish this credit to be enhanced. For most research workers facilities for publication in this country already exist—the several Australian journals are able to record what has been done, sometimes in considerable detail, and Australian workers also realize that workers in other parts of the world will not look to Australia and to Australian journals unless those journals contain material that will attract their attention. There is one class of worker, or perhaps we should say one class of work, for which arrangements are not at present adequate. The more extensive type of work generally published in monograph form can, of course, be produced in this country, but, as a rule, authors have to make their own arrangements and undertake the publication themselves, though sometimes the institute or organization for which they work may do it for them. Some workers can afford to publish their own monographs and in some instances, no doubt, they receive a reasonable return from their outlay.

For some time it has been felt that arrangements should be made for workers in Australia who are not able to pay for their own monograph publications. It was about twelve months ago that a proposal was brought before the Federal Council of the British Medical Association in Australia that a monograph fund should be established, and that this should be controlled and used for the benefit of authors who needed help. The Federal Council appointed a subcommittee to go into the question and to draw up a series of suggestions. These were put before the last meeting of the Federal Council held in Adelaide in October, 1953, and the suggestions were adopted. As a result, the Federal Council Monograph Fund is now an established fact, and its trustees are Dr. A. J. Collins, Dr. A. J. Murray and Dr. W. F. Simmons. The Federal Council resolved that a letter of appeal for donations for the fund over the signature of the President should be published in THE MEDICAL JOURNAL OF AUSTRALIA. The President has forwarded the following letter:

The Editor,
THE MEDICAL JOURNAL OF AUSTRALIA.

FEDERAL COUNCIL MEDICAL MONOGRAPH FUND.

Sir,

From time to time papers of unusual value which have been submitted to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, have not been accepted because of their length. Sometimes the letterpress has been unduly long, and sometimes the number of illustrations has been very large. To attempt the publication of an abstract of these contributions would deprive them of much of their value. Such contributions are suitable only for publication in the form of monographs. Few authors are in a position to undertake the publication of a monograph, and publishers in Australia cannot be expected to undertake what would be a hazardous publication. However, it is not easy for an Australian author to submit the text of a monograph to a publisher in the United Kingdom or the United States.

Having regard to the fact that the promotion of the medical and allied sciences is one of the objects of the British Medical Association, and with a view to assisting Australian authors in the publication of their works, the Federal Council at its meeting in Adelaide on October 26, 1953, decided to establish a fund, the Federal Council Medical Monograph Fund, and to invite donations to the fund.

The object of the fund is the publication of monographs of a high standard on the medical and allied sciences on behalf of authors who are unable to bear the cost of publication. The monographs will be edited and published by the Australasian Medical Publishing Company, Limited, no charge being made by the Company for the editing.

Proceeds of the sales of monographs will be paid into the fund unless otherwise determined by the trustees.

I am sure there is no need for me to stress the worthy object of the fund, and I therefore confidently appeal to members of the Association throughout Australia for donations to the fund.

Yours, etc.,

A. J. COLLINS,
President, Federal Council of the British Medical Association in Australia.

135 Macquarie Street,
Sydney,
December 18, 1953.

The report by the subcommittee presented to the last meeting of the Federal Council was published in the issue of December 19, 1953. It should perhaps be pointed out that monographs offered for publication by the fund will be scrutinized by the trustees and by the Editor of THE MEDICAL JOURNAL OF AUSTRALIA, and that they will determine whether the advice of special referees is neces-

sary. Monographs will be accepted for publication only on the advice of specially selected referees. It is intended that the *corpus* of the fund shall be used, and that, as a general rule, the money derived from sales of monographs shall be paid into the fund. This new move of the Federal Council must appeal to every scientifically minded member of the medical profession. After all the publication of the results of research is part of research—research is not complete unless what has been learned is made known. In establishing this fund the Federal Council has made an attempt to further research in Australia. Donations to the fund are invited from Branches of the Association, from the members of the Branches, from scientific, non-medical organizations and from scientifically minded members of the community.

Current Comment.

FASCINATION AS A CAUSE OF ERROR AMONG AEROPLANE PILOTS.

AN interesting paper, entitled "Fascination: A Cause of Pilot Error", has recently been published by B. Clark, M. A. Nicholson and A. Graybiel.[1] These authors state that analyses of accidents during aeroplane flights have led most students of aviation safety to the conclusion that 80% or more of all aircraft accidents are the result of "pilot error". They state, however, that this stock phrase affords little or no understanding of the basal causes of these accidents. They studied the nature of the human being flying the aircraft and his reactions to the different situations encountered. One specific factor which may contribute to accidents is "fascination". This is defined as a condition in which a pilot fails to respond adequately to a clearly defined stimulus-situation in spite of the fact that all of the necessary cues are present for a proper response and the correct procedures are well known to him. Fascination has also been described as a state of narrowed attention associated with excessive concentration on some object or task with resulting loss of voluntary control over response. It appears that instructors in formation flying have described experiences in which the student pilot, "flying wing on another plane", failed to manœuvre in order to avoid certain collision. This occurred under circumstances which posed no problem in flying skill. As a preliminary step to their study the authors interviewed 25 instructors of formation flying because it was thought that this particular type of flying might be conducive to experiences with fascination. A *questionnaire* was then drawn up and submitted to flight students. The students were assured that all their statements would remain confidential and that the results would be used for research purposes only. The *questionnaire* was submitted to 226 naval aviation students who were approaching the end of their basic flight training, and to 276 students in advanced training. Of the latter group, 77 were in the final stages of training. No less than 107, or 39%, of the advanced students and 79, or 35%, of the basic students wrote a description of one of their own experiences with fascination. Nineteen advanced students and 13 basic students described fascination as experienced by another person. This gave a total of 218 sets of replies available for analysis. It was found that fascination could be divided into two categories. Type A fascination was fundamentally perceptual in nature: the individual attended to one aspect of the total situation to such a degree that he excluded other important items from his perceptual field. The field of attention became so greatly restricted that important stimulus-variables were not perceived at the time; therefore the subject did not react appropriately, although he might later recall that the stimuli had been present. Of the fascination experiences described by advanced students 75% and of those described by basic students 66% fell into this category. In type B fascination the individual might perceive all the significant aspects of the total situation but still fail to make proper voluntary response. The effects, rather than being perceptual, appear to have elements in common with compulsive types of behaviour or with the blocking which is commonly associated with anxiety states and the early stages of learning. Of the fascination experiences of the advanced students 16% fell into this category, and 25% of the basic students' totals also came within it. The instructors were asked what they believed were the factors which contributed to fascination. They had a number of explanations to offer. Generally speaking, they recognized that there was no single simple cause, but that probably at least two or three factors were of importance in any one case. Some of the factors which they mentioned were tiredness, fear, difficulty in shifting attention, the stage of training, mechanical flying and mental blocks.

In the discussion the authors point out that the term fascination does not represent a single clearcut entity with a well-defined ætiology. Like the term vertigo, it covers a fairly wide variety of experiences. The reports of fascination from 502 student pilots suggest that it is more complex than its definition would indicate. It is pointed out that suggestions made for the handling of this manifestation are more applicable to type A than to type B, which is very much more complex. The first suggestion is that whenever possible additional emphasis should be placed on teaching the student to shift his attention from one significant thing to another in his visual and auditory field. In the second place, techniques to reduce tenseness on the part of the student should reduce the occurrence of fascination. Thirdly, a knowledge of what fascination is and some methods of dealing with it should aid in reducing its occurrence. In the fourth place, some instructors thought that fear was an important contributor in some instances, and the authors think that this appears to be logical in the light of the disorganized behaviour which is characteristic of certain fear reactions.

This subject has been mentioned chiefly for its interest, but also because it might be worth while to consider whether an investigation such as that reported could be devised in connexion with such a human activity as motor-car driving. The flying of aeroplanes is a much more difficult and hazardous activity than the driving of motor-cars, but the latter is accompanied by so many accidents which are the result of so much human frailty that it would be useful to discover whether such a phenomenon as "fascination" could not be described in connexion with it. If this was possible, some suggestions for the occasional or continuous indoctrination of motor-car drivers might be devised. As it is, in certain States drivers of motor-cars who have been guilty of some small breach of the driving regulations are required to attend a lecture by a member of the Traffic Department. If some study in connexion with motor-car driving similar to that which has been undertaken for aeroplane flying could be devised, further means of reducing the toll of motor-car accidents might be set in train.

[1] *J. Aviation Med.*, October, 1953.

SURGICAL TREATMENT OF MITRAL STENOSIS IN PATIENTS OVER FIFTY.

THE relative simplicity of the operation of mitral commissurotomy has widened its scope, though this statement does not imply that it can be safely attempted and carried out except by skilled and experienced surgeons. For some time before thoracic surgeons began this work considerable interest had been shown by physicians and pathologists in the significance of Aschoff bodies in the hearts of persons dead of conditions not necessarily related to acute rheumatic fever. An assumption of an earlier day suggested that the histological evidence of rheumatic lesions was to be expected only in young subjects, but mere age could not

be taken as a contraindication of the existence of Aschoff nodes. This being so, it was realized that when surgical relief can be given to the mechanically disabling lesion of mitral stenosis it need not be denied to those who are under the risk of recurrence of exacerbations of cardiac rheumatism. Further, as the subacute or chronic tissue changes alone produced more interference with the efficiency of the heart, it became evident that if operation was to be undertaken it was best done while the cardiac condition was reasonably stabilized. This attitude was not pressed too far, however, and natural hesitation was felt in subjecting patients to operation whose risk of thromboembolism was considerable. Recently an article has been published giving details of twenty patients who have had the operation of mitral commissurotomy performed successfully in spite of their being over the age of fifty years. These were taken from a group of 400 patients suffering from mitral stenosis and aged from fifty to sixty-one years. The stated purpose of the procedure was to widen the constricted orifice, to restore movement to the valve leaflets and to prevent future thrombosis and embolism. The patients in this series were followed for a period of six months to two years. The authors, O. H. Janton, R. P. Glover and T. J. E. O'Neill, claim that selected patients of this age can be safely submitted to operation without unusual morbidity or mortality, and with a significant gain in functional capacity of the heart.[1] All the patients were severely incapacitated, and 18 had suffered varying degrees of congestive cardiac failure. Embolism had occurred in five of the series. At the time of operation exertion produced definite dyspnœa, and three patients were considered to be "bad risks" on account of considerable enlargement of the heart. In eleven of the patients the mitral stenosis was "pure" in type, but in the remainder there were also signs of mitral insufficiency. All patients had some degree of cardiac enlargement, and twelve had auricular fibrillation of permanent type—that is to say, not paroxysmal. Two of the patients died some months after operation, and three others showed no post-operative improvement. Two patients suffered cardio-vascular accidents in the post-operative period. The authors admit that their series is too small to be statistically significant, but they consider that the mortality and morbidity were not in excess of those observed in groups of lesser age, and sum up that fifteen patients showed significant benefit from operation. Since writing their article they have added to their series and now report that out of a total of 35 patients the post-operative mortality was three. They remark that the most valuable guide in the selection of cases suitable for commissurotomy is the size of the heart. There are a number of interesting points to consider in this extension of mitral valve surgery to the older age groups; perhaps by these studies extension of our pathological knowledge of mitral stenosis may be stimulated to some extent.

CHEMOTHERAPY FOR RENAL TUBERCULOSIS.

ESPECIALLY when used as a preliminary to surgery chemotherapy has an established value in the management of renal tuberculosis. Nevertheless, it has definite limitations, which longer experience is helping to define. The drugs in most general use are streptomycin, PAS and isoniazid (isonicotinic acid hydrazide). All three are included in a report by P. Lerman and L. L. Spivack[2] on 458 cases of genito-urinary tuberculosis treated by chemotherapy alone by the Research Group of the Veterans Administration of the United States Army and Navy. The study is now five years old. The objective has been to try to determine the optimum long-range dosage plan for streptomycin and other new anti-tuberculosis drugs. Symptomatic improvement has been impressive, mostly because of the healing of bladder ulcers. Improvement was noted even in patients whose urine still contained tubercle bacilli. The progress of tuberculous cavitation appeared to be halted in both small and massive lesions, as judged by serial pyelograms. However, strictures of calyceal necks or of ureters sometimes occurred during treatment. This led to a policy of checking by excretion urograms every four months; if ureteric strictures were discovered early, the ureters could be successfully dilated and usually stayed open thereafter. Treatment was judged successful only if tubercle bacilli disappeared from the urine as ascertained by culture; this was a most demanding criterion. Patients who had active lesions in the genitalia and kidneys at the same time were the most difficult to bring to this standard. Combined therapy (streptomycin, one gramme every third day, with PAS, 12 grammes daily) was superior to treatment with streptomycin alone. With this intermittent use of streptomycin, toxicity was less and tolerance greater. Duration of treatment has been lengthened to at least one year in view of the fact that the combined intermittent treatment greatly defers the development of drug resistance. Inoperable bilateral renal tuberculosis was treated with up to three years of intermittent combined therapy. Five years of follow-up appear to justify the conclusion that such chemotherapy can at least modify the lethal course of renal tuberculosis.

During the past year use has been made of isoniazid (isonicotinic acid hydrazide), which *in vitro* at least is 600 times as powerful as PAS in killing tubercle bacilli and is also more powerful than streptomycin. Like streptomycin, isoniazid causes gradual improvement in the cystoscopic appearance of vesical tuberculosis lesions and can make the urine sterile for tubercle bacilli in some cases. It is an excellent drug for treatment in streptomycin-resistant cases. However, when used alone, isoniazid has the same limitations as streptomycin, *plus* a danger all its own. The presence of large amounts of necrotic tissue render the drug ineffectual in sterilizing urine from massive kidney lesions. Resistance to the drug may be developed by tubercle bacilli in two to eight weeks. In uræmic patients the drug will accumulate in the blood and may become a convulsant in high concentrations. When it is used in cases of advanced renal disease, therefore, the blood level of the drug should be tested regularly. In view of the development of resistance, it may prove desirable to give this drug intermittently, and probably in combination with PAS and streptomycin. The tentative dosage plan which is being investigated at present is as follows: streptomycin, one gramme in one injection every third day, *plus* isoniazid, 150 milligrammes every twelve hours. In addition, if the patient's bowels are not made too loose or too tympanitic, PAS is given in three-gramme doses every six hours.

Another report, by S. Scher,[1] on the use of streptomycin and PAS in the treatment of advanced renal tuberculosis, though based on only four cases, is thought to be of sufficient importance to be published at this stage. These cases illustrate the point that the following complications may occur after treatment of renal tuberculosis with streptomycin and PAS: (i) dilatation of the upper part of the urinary tract with reflux up the ureter (there is no apparent stricture at the uretero-vesical junction); (ii) further contracture of the bladder; (iii) stricture-formation in the tuberculous ureter along its course. Scher states that these changes have never been noted in early cases of renal tuberculosis, but only in advanced cases in which the structures concerned are already extensively involved. It is doubtful if secondary infection plays any important part. The changes produced by streptomycin and PAS resemble closely those found occurring naturally in advanced renal tuberculosis with the passage of time. The only difference is that these fibrotic and contractural changes occur a great deal more quickly under the influence of these drugs. This comes about by the very efficiency of streptomycin and PAS in their destruction of tubercle bacilli and consequent liberation of toxin, with inflammatory reactions leading to fibrosis. As regards circumvention of these complications, there has been speculation on the use of cortisone together with streptomycin and PAS to reduce the inflammatory reaction which leads

[1] *Circulation*, September, 1953.
[2] *J. Urol.*, June, 1953.

[1] *Brit. J. Urol.*, June, 1953.

to fibrosis. However, there is danger in using cortisone in the presence of tuberculosis, and it is probably wiser not to use streptomycin and PAS in the treatment of advanced renal tuberculosis.

ACUTE INFECTIOUS HÆMORRHAGIC FEVERS IN THE SOVIET UNION.

IN July, 1951, a disease broke out amongst the troops in Korea which was known as epidemic hæmorrhagic fever. It was subsequently described in two articles in this journal, one by Wing-Commander N. M. Kater in the issue of December 15, 1951, and the other by Major Donald D. Beard in the issue of March 1, 1952. It was described by Kater as an acute infectious disease of virus ætiology, characterized by an abrupt onset with chills, high fever, headache, myalgia, vomiting, abdominal pain, albuminuria, leuchæmoid leucocytosis and hæmorrhagic phenomena, increasing with defervescence of the fever. It was said then to be transmitted by the mite *Loelaps Jettmari Vitzthum*, the host of the mite and the probable reservoir of the disease being the field rodent *Apodemus agrarius*. It appeared that the Japanese had first come into contact with the disease in the Songo district of northern Manchuria in 1939. It was a disease unknown to the Japanese in either Korea or Japan. Further consideration established the fact that several outbreaks of an undiagnosed fever among the Japanese troops in the years 1935-1938 in northern and north-eastern Manchuria were the same disease. It seemed probable that the 1951 outbreak was the result of its being brought into the area by Chinese Communist troops. The name "epidemic hæmorrhagic fever" had been given to the disease by the Japanese, but according to J. E. Smadel in the foreword to a recent monograph by Captain D. Carlton Gajdusek,[1] the disease had also been observed by the Russians and given by them the name "hæmorrhagic nephroso-nephritis". Prior to the 1951 outbreak, the only original scientific articles dealing with epidemic hæmorrhagic fever were to be found in Japanese and Russian publications, but since that time a number of papers on the subject have appeared in English journals, and several summaries of the foreign literature have appeared in the English language. Smadel states that during the course of the studies on epidemic hæmorrhagic fever it became evident that this disease was only one of a number of similar distinct hæmorrhagic fevers which occur in various parts of the Soviet Union. In order that information on these other hæmorrhagic fevers might be made available to the American groups working on the disease in Korea, Gajdusek summarized the relevant Russian scientific publications so far as they were available in American libraries, and the present monograph is the result.

Gajdusek states that during the past two decades medical investigators in the U.S.S.R. have encountered a group of acute infectious diseases which is characterized by the presence of an alarming hæmorrhagic syndrome in a high percentage of the cases, and by distinct geographic localization of each of the separate diseases. These hæmorrhagic fevers have been reported from a wide belt extending across the southern and central regions of the Soviet Union, from Bukovina to Vladivostok, and expeditionary teams of medical scientists have been sent to study the clinical course, pathology and epidemiology of these diseases, to attempt to isolate the ætiological agents, and to discover the vectors of the disease and their reservoirs in nature. In some instances investigators have met with remarkable success; they have succeeded in isolating the responsible microbial agent, in elucidating the epidemiology and in developing therapeutic, prophylactic and specific diagnostic procedures for the maladies. In the review two main groups of diseases are discussed. The first are the so-called hæmorrhagic fevers: Crimean hæmorrhagic fever, Omsk hæmorrhagic fever, Bukovinian hæmorrhagic fever, Uzbekistan hæmorrhagic fever, and Far Eastern hæmorrhagic fever or endemic hæmorrhagic nephroso-nephritis (the epidemic hæmorrhagic fever of the Korean front). The second group of diseases are described as mycotoxicoses: alimentary toxic aleukia, poisoning with "drunken bread", stachybotryotoxicosis, and dendrodochiotoxicosis. Gajdusek refers also to a group of acute infectious hæmorrhagic diseases occurring in or near Soviet Central Asia, and to *nephropathia epidemica*, a disease of northern Scandinavia with much similarity to Far Eastern hæmorrhagic fever.

These hæmorrhagic fevers are described as acute, febrile capillaropathies with evidence of autonomic nervous system involvement caused by viruses which are maintained in an extra human cycle in nature, and which involve man only occasionally and accidentally. They are predominantly seasonal in occurrence. In four of the diseases an ixodid tick has been incriminated as the vector and probable long-term reservoir of the viruses in nature. Clinically, pathologically and epidemiologically these diseases are similar, although the experimental investigation of the ætiological agents of Crimean, Omsk and Uzbekistan hæmorrhagic fevers, all of which have been isolated, has revealed them to be distinct entities. Omsk and Bukovinian hæmorrhagic fevers may be caused by the same or a closely related agent, and the Uzbekistan and the Crimean viruses may also be closely related. The number of distinct disease entities of the hæmorrhagic fever group occurring in Soviet Central Asia remains uncertain. Alimentary toxic aleukia, the first of the group of mycotoxicoses, is a very different type of disease from those already referred to. It is thought to be caused by the toxin produced by a fungus, *Fusarium sporotrichioides*, infecting grain which has been left to overwinter in the fields. Gajdusek states that, since it must enter into the differential diagnosis of the other diseases, and since it is a disease previously undescribed in American literature, it is also being reviewed. Three other mycotoxicoses of the U.S.S.R.—namely, poisoning with "drunken bread", stachybotryotoxicosis and dendrodochiotoxicosis—are also briefly reviewed.

After each chapter dealing with an individual disease a comprehensive bibliography is presented of the references which deal with the disease under discussion. This, with certain limitations, makes the monograph definitive; but it is pointed out that since the published writings of Russian scientists are the only available source of information for all the diseases described except the Far Eastern hæmorrhagic nephroso-nephritis, the reviews are necessarily only as accurate and as complete as is the available Russian literature on the subject. Further details of these diseases do not concern us now. They are available in the monograph for those who are interested. It may be noted, however, that the Russians appear to have evolved no specific treatment for any of the hæmorrhagic fevers. The treatment described is symptomatic and supportive, as it was for epidemic hæmorrhagic fever when Kater and Beard wrote on the Korean outbreak.

[1] "Acute Infectious Hemorrhagic Fevers and Mycotoxicoses in the Union of Soviet Socialist Republics", by D. Carleton Gajdusek; 1953. Washington: Walter Reed Army Medical Center. 9½" x 6", pp. 148, with seven text figures and two maps. Price: 60 cents.

THE AUSTRALIAN RED CROSS SOCIETY APPEAL.

THE Australian Red Cross Society is making its March appeal to the people of Australia. It is with the greatest pleasure that we comply with the request of the Society to bring this appeal to the notice of readers of the journal. Medical practitioners, as far as the Red Cross Society is concerned, are in a somewhat different category from that of other members of the community. They know what the Society does, they know what it stands for, and they make use of its facilities whenever they feel need of them. In connexion with this appeal we call to mind a brochure published by the Society in 1941. It set out the story of the Red Cross and was written by Joan and Daryl Lindsay. We recall that since the Geneva Convention was signed the provisions have been extended and assistance has been given by the Red Cross Society in such national calamities

as famines, typhoons and earthquakes. We also recall that the Society has helped to stem the ravages of such diseases as leprosy, tuberculosis and yellow fever. Many Australians will remember with gratitude what the Red Cross Society was able to do for them in discovering the whereabouts of and in helping prisoners of war in the last great conflict. In Australia at the present time the service of the Society that is best known is the provision of blood for the purpose of transfusion. The appeal of the Society states that according to the voluntary donor system under which it works, a pint of whole blood costs 32s. 6d. to produce. This entails the expenditure of a vast amount of money every year. As blood transfusion is becoming more and more widely used, the income of the Society needs to become larger and larger. It has been claimed that almost every Red Cross activity is directly or indirectly connected with the medical field. Among the lesser known services may be mentioned such activities as the provision of rest rooms at public hospitals, the supply of canteens for out-patients, assistance at country hospitals, handicraft services at some hospitals and library services at others. For the doctor in private practice the Red Cross is of considerable assistance, because such appliances as bed pans and wheel chairs are available on loan to patients. Even the welfare department in helping to solve an economic problem for an ex-serviceman is in fact contributing to his well-being and possibly helping him to avoid a mental or physical breakdown. This Red Cross appeal is commended with the greatest earnestness to all members of the medical profession.

HEAT-PROCESSED FOODS AND EXPERIMENTAL DENTAL CARIES IN RATS.

ONE of the major public health problems in Australia today is the prevention of dental caries. There is no doubt that the causes of the widespread incidence of dental caries are to be found in the present-day diet pattern. Amongst those factors that have been thought to predispose to dental caries is the consumption of foods containing refined sugars and flours. It has been thought that foods of this nature are particularly harmful if their consistencies are such that particles tend to adhere to the teeth for large periods and to undergo acid fermentation.

During the past few years a number of diets cariogenic for laboratory rats have been developed. These include the "coarse particle" diet and the "refined diets" containing large amounts of sugar. These diets produce a type of dental caries that for the most part originates in the fissures and on the occlusal surfaces (that is between the teeth). Many people have questioned whether this type of caries is a true species analogue of human dental caries. Dental caries in humans differs from that produced by most experimental procedures in rats in that the lesions tend to develop on the proximal buccal and lingual surfaces of the teeth. A discovery of great interest to those interested in the relationship of diet and dental caries is reported by F. J. McClure.[1] It was found by this worker that white rats fed diets low in sugar, but containing cereals which had been dried, toasted, and ground to a fine powder, developed a high incidence of dental caries. The heat treatment of the cereals was rather severe and evidently greatly affected the biological value of the proteins, because despite the fact that vitamins *A*, *D* and the *B* group were added to the diet, growth was much below normal. This is in accordance with the well-known fact that comparatively severe heat treatment does affect the protein value of cereals.

In a more recent article F. J. McClure and J. E. Folk,[2] following up this earlier work with heat-processed cereals, have investigated the cariogenicity for rats of diets containing various heat-processed skim-milk powders.

The diets, which were finely powdered, contained 35% of one of the milk powders being tested, 18% glucose, 45% starch, and 2% dried liver. Concentrated vitamins *A*, *D* and *E* were given weekly, and the diets were fed from weaning. At ninety days the rats were sacrificed and the extent of caries that had developed was noted. It was found that, as in the case of heat-treated cereals, the type of caries seen closely resembled human caries.

Spray-dried milk powder, which is subject to a minimum amount of heat treatment during processing, was definitely less cariogenic than roller-dried milk powder, 12% of rats being affected with 0·3 carious tooth per rat in the case of spray-dried milk, whereas 51% of the rats were affected with 2·7 carious teeth per rat in the case of roller-dried milk. When the spray-dried milk was spread to a depth of half an inch in a sealed pan and heated in an autoclave for fifteen minutes at approximately 121° C., its cariogenicity increased, 40% of rats being affected with 2·63 carious teeth per rat. Similar heat treatment of roller-dried milk increased its cariogenicity to 74% of carious rats with 3·9 carious teeth per rat. One finding of great interest was that rats fed roller-dried milk grew at approximately the same rate as rats on spray-dried milk, although rats fed roller-dried milk showed more than four times as much caries, with an average score for caries more than ten times as severe as rats fed spray-dried milk. McClure and Folk point out that "these results on growth as compared with cariogenicity seem to suggest therefore that the cariogenic factor is possibly not the same as the growth inhibiting factors".

It would be unwise to assume that these results demonstrating the effect of heat processing of foods on experimental rat caries can be directly applied to human dental caries. Nevertheless the fact that the type of caries produced (that is, affecting the proximal buccal and lingual surfaces) more closely resembles human caries than any experimental rat caries hitherto produced, suggests that these observations may be of special importance. There is ample evidence that human caries can be prevented by avoiding diets that contain refined sugary foods, cakes and sweet biscuits, and choosing instead diets that contain vegetables, fruit, nuts and wholemeal bread. Unfortunately it has not yet been possible to define more clearly the dietary factors responsible for producing caries in humans, and to indicate those that are most harmful. It is apparent that anticariogenic diets are difficult to achieve under the existing social and cultural conditions in Australia. It is possible that from McClure's work there may emerge a dietary principle that will lead to the formulation of more generally accepted anticariogenic diets. It is evident that investigators in the field of nutrition have many surprises in store for them. We await further developments of this early work with much interest.

[1] *Science*, 116: 229.

[2] *Proc. Soc. Exp. Biol. & Med.*, 1952, 83: 21.

THE QUEEN IN NEW ZEALAND.

ONE of the "Peripatetic Correspondents" of *The Lancet* has written from New Zealand. Although the "Peripatetic Correspondents'" column is headed "In England Now", this writing from New Zealand will be gladly accepted. The correspondent writes as follows about the Queen: "Of course we in New Zealand have all been wrong in our assessment. Hitherto we have had only the verbal description, the static picture, and our imaginations. We have been diagnosing on the case-notes without the patient. She is much more beautiful than we thought. She is much more regal. She is much more attuned in sympathy to her people than we thought possible. She has a measured dignity that is more symbolic of her status than is a crown or a throne. Merely by her presence she has changed loyalty to enthusiasm and replaced respect by affection." We have no doubt that a statement such as this will hold good wherever Her Majesty travels in the Commonwealth of Australia.

Abstracts from Medical Literature.

MEDICINE.

Blood Regeneration After Blood Loss.

D. H. COLEMAN, A. R. STEVENS, JUNIOR, N. T. DODGE AND C. A. FINCH (*Arch. Int. Med.*, September, 1953) have calculated, using standard techniques, the rate of regeneration of hæmoglobin after repeated phlebotomies in normal subjects and patients with depleted and increased iron stores. They state that blood production is proportional to the amount of available iron, whether derived from iron stores or from iron administration. People with normal findings in the peripheral blood may have depleted stores of iron, and bleeding results in little or no increase in blood production. Adequate available iron permits an acceleration of hæmopoiesis to two or three times the normal rate. Depleted iron reserves may delay recovery from a 500-mil phlebotomy for from two weeks to four months. When supplementary iron (1·0 to 1·5 grammes of ferrous sulphate daily) is given, phlebotomy may be performed every two weeks without the production of significant anæmia.

Treatment of Spasticity in Paraplegia.

S. STELLAR (*Arch. Neurol. & Psychiat.*, March, 1953) describes a method for relieving spasticity in paraplegics by intrathecal injections of alcohol. He states that there are no serious contraindications to the procedure, provided certain criteria are fulfilled—namely, the patients should have stationary spinal cord lesions with no useful voluntary motion in the legs, together with severe spasms and spasticity. A modified technique of alcohol injection is described. The author states that the relief of the spasticity is immediate and permanent, and beneficial effects on the bladder, ambulation and the attitude of the patient are likewise brought about.

Coronary Vasodilators in Clinical Practice.

H. I. RUSSEK, K. F. URBACH, A. A. DOERNER AND B. L. ZOHMAN (*J.A.M.A.*, September 19, 1953) report clinical studies with coronary vasodilator drugs for the relief of Heberden's angina. They studied 52 patients with this syndrome whose electrocardiographic response to exercise was constant when recorded from day to day. Glyceryl trinitrate favourably influenced the electrocardiographic abnormalities brought about by exercise in every case and was therefore used as the reference drug. The following drugs were studied: glyceryl trinitrate, papaverine hydrochloride, ethyl alcohol, aminophylline, "Roniacol" (β-pyridyl-carbinol tartrate), tolazoline ("Priscoline") hydrochloride, tetraethyl ammonium chloride, octyl nitrite, dioxyline ("Papaveril") phosphate, "Visammin" (khellin), heparin, bishydroxycoumarin (dicoumarol), pentaerythritol ("Peritrate") tetranitrate and morphine. The following drugs were effective in preventing or lessening electrocardiographic abnormalities on exercise: glyceryl trinitrate, 1/150 to 1/100 grain given sublingually; papaverine hydrochloride, 1·0 to 2·0 grains given intravenously, or 1·5 to 8·0 grains given orally; pentaerythritol tetranitrate, 10 to 20 milligrammes. With the last-named drug an improved response was found as long as four to five hours after administration. The remaining drugs did not influence significantly the electrocardiogram after exercise. Ethyl alcohol in doses of one to two ounces did, however, prevent or reduce the severity of anginal pain. Morphine had the same effect. The authors conclude that of the drugs tested glyceryl trinitrate, papaverine and pentaerythritol tetranitrate alone appear worthy of continued clinical use as vasodilators in the management of *angina pectoris*.

Poliomyelitis: Studies on Temperature Regulation.

I. A. BROWN, A. B. BAKER AND S. CORNWELL (*Arch. Neurol. & Psychiat.*, March, 1953) describe studies made on 115 patients with bulbar poliomyelitis to determine whether any of the cell groups were specific in the regulation of body temperature. In 12 cases prolonged hyperthermia was found; in all these, cell damage was most severe in the rostral portion of the hypothalamus, involving chiefly the supraoptic, paraventricular and lateral nuclei. Of these nuclei, only severe damage to the paraventricular nuclei was exclusively associated with excessive temperature elevations, and this nuclear group was believed to play a most important role normally in the lowering of body temperatures. In nine cases there was clinical hypothermia. In all these the lateral and medial hypothalamic nuclei were severely damaged. The lateral nuclei were also involved in cases of hyperthermia; so only the medial group was considered specific for elevation of body temperature, with damage to this nuclear group resulting in hypothermia. The lateral hypothalamic nuclei were likewise shown to have an important accessory role in the regulation of body temperature; their damage produced a poikilothermic state with either abnormal heating or cooling. The posterior hypothalamic group was not severely involved in the cases showing temperature disturbances, and does not seem to play a great role in temperature regulation. The authors conclude that because of the frequent involvement of the hypothalamus in poliomyelitis, resulting in instability of temperature control, particular attention must be given to the regulation of body temperature in all patients with bulbar poliomyelitis, in order to prevent or minimize excessive temperature elevations which may complicate the care of these acutely ill patients.

Radioactive Iodine and Cancer of the Thyroid.

T. W. RAWSON, J. E. RALL AND J. ROBBINS (*Arch Int. Med.*, September, 1953) summarize their experience in the uses and misuses of radioactive iodine in treating cancer of the thyroid. They state that natural avidity for iodine of the great majority of primary and metastatic thyroid carcinomata is low. When the malignant tissue can be removed by a competent surgeon, surgery is the treatment of choice. In treating metastatic carcinoma, for example, in lungs and bones, the thyroid is first removed surgically, and tracer studies with radioiodine are carried out every four to six weeks for three to six months. Thiouracil in doses of 1·0 to 1·5 grammes daily is then given for six to eight weeks, and another tracer test is made. If the urinary excretion in ninety-six hours is less than 40% of the dose administered, the patient is a candidate for treatment. A second and larger dose of I^{131} is then given, after which daily urinary excretion is determined, counts are made over the tumour at forty-eight hours, and the blood level is determined daily for at least seven days and plotted graphically. From the data an attempt is made to determine whether a cancericidal dose of I^{131} can be given without doing the patient serious harm. A safe but maximum dose of I^{131} is then given, and the same determination is made as for the test dose. The blood count is followed for three weeks after treatment. With these methods it has been shown that a large percentage of thyroid carcinomata can be made to increase their avidity for iodine and so be rendered susceptible partially or wholly to a maximum dose of I^{131}. Of 28 patients treated, 10 have shown sustained objective improvement. The authors state that radioactive iodine should be used only when the disease cannot be dealt with surgically and when the avidity of the thyroid tissue is great enough or can be made great enough to enable a cancericidal dose to be delivered without serious damage to extrathyroidal tissues. In treatment it is particularly harmful to give so little I^{131} that it destroys function without being lethal to thyroid cells.

Aids to Pneumothorax Treatment.

G. BIRATH (*Dis. Chest*, September, 1953) has found from the study of large numbers of comparable cases that the administration of para-aminosalicylic acid and dihydrostreptomycin during the initial stages of pneumothorax treatment for pulmonary tuberculosis reduces the incidence of pleural effusion, even after adhesion cutting. Pleural effusion when formed tended to be less persistent and empyema was not seen.

Fire Fighting and Heart Disease.

N. E. REICH (*Dis. Chest*, September, 1953) states that a study of mortality by occupation amongst white male insurance policy holders in New York shows that city firemen have the highest standardized relative index of mortality (125) for the principal cardio-vascular diseases. Hypertension, coronary thrombosis, the anginal syndrome and manifestations of accelerated atheromatous changes occur with more than ordinary frequency in firemen.

Meningioma of Anterior Clinoid Process and Unilateral Loss of Vision.

ALFRED UHLEIN AND ROBERT D. WEYAND (*Arch. Ophth.*, March, 1953) state that in a review of 310 cases of unilateral loss of vision, lesions of the optic nerve or visual pathways accounted for 108 cases, and of these 15 were due to meningioma of the anterior clinoid process. A complete investigation including X-ray examination of the skull, charting of visual fields and ophthalmoscopic examination is of importance so that early diagnosis may be made and early treatment instituted. The authors have treated 52 patients with meningioma of the

anterior choroid process with an operative mortality of 32·7%. They state that females are more prone than males. The average age at time of diagnosis was forty-five years. In 30 of the cases loss of vision was the initial symptom. Other symptoms were puffiness of one eyelid, anosmia, mental change, photophobia, diplopia, episodes of giddiness and weakness of the legs. Headache was a common symptom; it was frequently retroorbital and associated with nausea. Unilateral exophthalmos was seen in 12 cases. Unilateral optic atrophy was the commonest ophthalmoscopic finding. Visual fields were found to be altered in all but two cases. X-ray examination of the skull suggested the presence of an intracranial tumour in 36 cases. The authors believe that in every case of unilateral visual impairment, neurosurgical consultation, X-ray examination of the skull and accurate performance of tests of visual fields should be carried out so that early diagnosis can be made.

Amyotrophic Lateral Sclerosis.

T. LAWER, JUNIOR, AND M. G. NETSKY (*Arch. Neurol. & Psychiat.*, February, 1953) give a detailed illustrated clinico-anatomical study of 53 cases of motor neuron disease, comprising two cases of progressive spinal muscular atrophy and 51 cases of amyotrophic lateral sclerosis. Their analysis of the cases offers confirmation of the fact that the motor neuron disease group includes progressive spinal muscular atrophy, primary lateral sclerosis, amyotrophic lateral sclerosis and progressive bulbar palsy.

Pulmonary Consolidation in Primary Tuberculosis.

D. ADLER AND W. F. RICHARDS (*Thorax*, September, 1953) report 83 cases of collapse and collapse-consolidation occurring in the course of primary tuberculosis of the lung. The consolidation tends to resolve and streptomycin and PAS are not considered to be of value. The cause of the condition is thought to be the inoculation of tuberculous material in the lung of an allergic individual. The source of the inoculation is probably in the majority of cases from a tuberculous broncho-pulmonary gland which has perforated the bronchial wall.

Hæmangiomata of the Pons.

K. TEILMANN (*Arch. Neurol. & Psychiat.*, February, 1953) discusses the classification of vascular tumours of the central nervous system and describes in detail three cases of pontine hæmangioma. He also reviews the literature on the subject, including an analysis of 42 previously reported cases. He gives the principal clinical features of a characteristic case and describes the limited therapy available for these conditions.

Changing Incidence and Types of Heart Disease.

J. M. HUTCHESON *et alii* (*Am. Heart J.*, October, 1953) have compared the heart disease met with at a medical centre in Texas today with that of twenty-five years ago. The incidence of hypertensive heart disease is approximately the same as before, but that of arteriosclerotic heart disease has increased. The peak age-incidence of hypertension is ten years later than before. There has been a tenfold increase in the diagnosis of congenital heart disease. Syphilitic heart disease has conspicuously decreased and is now infrequent. Rheumatic heart disease has shown little change in frequency, but there has been less bacterial endocarditis. There has been a striking increase in the diagnosis of *angina pectoris*. The incidence of organic heart disease is greater in the Negro than in the white, but much less so than formerly.

Basal Ganglia Signs and Symptoms in Cerebral Tumour.

D. SCIARRA AND B. E. SPROFKIN (*Arch. Neurol. & Psychiat.*, April, 1953) report a series of 12 cases of cerebral tumour which showed extrapyramidal manifestations. A rhythmical alternating tremor was the commonest symptom, and others included athetosis, torsion spasm, posturing, rigidity and bradykinesia. The authors state that the differential diagnosis between Parkinson's disease and Parkinsonism with brain tumour must be made in a small number of cases; the age of the patient, duration and location of the extrapyramidal signs and other neurological signs and symptoms may facilitate the differentiation, and more definitive tests such as air studies may be necessary.

An Unusual Case of Progressive Bulbar Paralysis.

E. E. ROBERTSON (*Arch. Neurol. & Psychiat.*, February, 1953) gives a detailed report of a case of progressive bulbar paralysis in an adult in which there were unusual features—namely, a heredo-familial incidence and mental symptoms characteristic of organic intellectual deterioration. He points out that while each of these features has been reported separately in cases of motor neuron disease, he is not aware of any one case in which they have been concomitant. He concludes that the genetic basis is an autosomal dominant gene showing irregularity in expression, and that the accompanying mental symptoms are caused by a cortical extension of the disease process.

Fatal Asthma.

J. C. HOUSTON *et alii* (*Thorax*, September, 1953) discuss nine fatal cases of asthma and review the literature on the subject. They find that the prognosis of asthma is much worse when it begins after the age of forty years. Only two of their nine patients had been given morphine, but five had received paraldehyde, which has little effect on the respiratory centre. Extensive detachment of the ciliated epithelium of the bronchi was found in all cases at autopsy, and the lungs as a rule were dry and emphysematous with widespread obstruction of bronchi by mucus. The loss of the ciliated epithelium was thought to have an important bearing on the development and course of *status asthmaticus*.

Arterio-Venous Aneurysm of the Mid-Brain.

H. ASKENASY, H. WIJSENBEEK AND E. HERZBERGER (*Arch. Neurol. & Psychiat.*, February, 1953) report a unique case in which a thirty-six-year-old patient was found (by arteriography) to have a vascular malformation of the mid-brain. The patient had had two subarachnoid hæmorrhages, the second of which produced a curious mesencephalic syndrome consisting of three rare clinical signs and symptoms—retraction nystagmus, retraction of the lids and Parinaud's syndrome (disturbance of conjugate upward movements with pupillary abnormalities). The authors describe possible mechanisms for the production of the syndrome and review the literature on the subject.

Tic Douloureux of the Chorda Tympani.

SAMUEL ROSEN (*Arch. Neurol. & Psychiat.*, March, 1953) describes two cases of *tic douloureux* permanently relieved by section of the *chorda tympani* (via the tympanic route). He concludes that *tic douloureux* of the *chorda tympani* is a clinical entity, that tic-like pain in the ear may be abolished by section of the *nervus intermedius*, *chorda tympani* or glossopharyngeal nerve, and that the nerve responsible for the tic-like pain may be determined by differential electrical stimulation in the tympanic cavity.

Gargoylism.

ELMER V. KENNEALLY (*Am. J. Ophth.*, May, 1953) describes four cases of gargoylism with particular reference to the ocular manifestations. He states that the disease is believed to be a generalized condition in which almost all the tissues of the body are sites of an abnormal storage process involving glycogen, or glycogen in combination with protein. The syndrome is manifested by skeletal deformities and dwarfism, hepato-splenomegaly, retarded mentality, hirsutism and a variety of ocular signs. There is a high familial incidence, male and female are equally affected, and the age of onset in reported cases is five months to twenty-nine years. The head is large with prominent forehead and supraorbital ridges. The face is large with a wide interpupillary distance and a flat nasal bridge. The tongue is thick and fleshy, and the neck is short. The thorax is misshapen, and dorso-lumbar kyphosis is present. The abdomen is protuberant, and the liver and spleen are palpable. The authors describe other features which may occur in the complete syndrome. The most characteristic X-ray sign is to be found in the vertebræ of the lumbo-dorsal region. The affected vertebral bodies are wedge-shaped with the antero-superior portion deficient and the antero-inferior border forming a hooklike or "beaking" process. Specific ocular signs are recorded in 75% of cases. The interpupillary distance is increased. The eyebrows are bushy and coarse, and the globes are somewhat protuberant. Convergent strabismus is frequent. The cornea is cloudy; this state may be present at birth, but usually appears after the first year. At first the cloudiness is only a dulness of lustre, but later it manifests itself as a constant milky haziness. In several cases the corneal diameters are enlarged. The ocular tension has been found to be slightly raised in some cases, and buphthalmos has been erroneously diagnosed. Gargoylism is to be differentiated from rickets, Morquio's syndrome, von Gierke's disease, cretinism, mongolism, congenital lues, Kleppel-Feil syndrome, Sprengel's deformity and phenylpyruvic oligophrenia. Primary buphthalmos is to be differentiated.

Special Abstract.

STATIC ELECTRICITY IN HOSPITALS.

By courtesy of the Secretary (Industrial and Physical Sciences) of the Commonwealth Scientific and Industrial Research Organization, a copy has been made available to us of a bulletin on static electricity hazards in hospitals, issued by the Bureau of Mines, Department of the Interior, United States of America. The authors are P. G. Guest, V. W. Sikora and Bernard Lewis, all of the Explosives and Physical Sciences Division of the Bureau of Mines. Guest, an electrical engineer, and Sikora, a physical science aide, belong to the Physical Sciences Branch of the Division, and Lewis is a physical chemist and Chief of the Division. It is understood that the bulletin would normally be received only by the mines departments in the several States, some of the capital city public libraries and a few other libraries. In view of the importance of the material presented in this bulletin, and the necessity for its being made generally available, we present the following summary of the main points.

Introduction.

Many of the gases and vapours used in anæsthesia form explosive mixtures with oxygen or air. Sources of ignition for these mixtures always have existed in operating and anæsthetizing areas. When ether was first introduced, candles, gas lights and coal stoves caused fires and mild explosions of the vapour-air mixtures. Today the chief causes of ignition are electrical. Fires and explosions are still much too frequent, and because many of the mixtures are rich in oxygen, the explosions sometimes are very violent.

Obvious sources of ignition, such as electric power sparks and arcs in open motors, switches and receptacles, as well as exposed incandescent wires and hotplates, usually are recognized by hospital personnel and corrected. A source of ignition that is not so obvious to many is static electricity. Until quite recently the presence of this hazard in a large majority of anæsthetizing areas was not even suspected. However, numerous explosions—many of them fatal to patients—have been attributed with good reason to sparks from static electricity.

Static Electricity.

The material universe is composed of atoms, the outermost parts of which are composed of electrons. An outer electron may be detached from an atom in many ways. Detached electrons often manifest themselves in electrical phenomena, of which perhaps the simplest are those of static electricity. Static electricity is extremely common, as electrons can be detached and transferred from surface atoms through mere contact and separation of material bodies.

In certain materials, notably metals, electrons can move from atom to atom with considerable natural freedom; these materials are good conductors of electricity. Other materials, such as glass, stone, rubber, plastics and textiles, have molecular structures that offer great resistance to the flow of electricity; these are non-conductors or insulators. Opposition to the flow of electricity is expressed in units called ohms or megohms (1,000,000 ohms).

When dissimilar materials are pressed together, free electrons from the surface structure of one material may shift across the contact or interface to the other. If the materials are separated the new distribution of electrical entities probably will persist if one or both of the materials are non-conductors. The object that acquires extra electrons is said to have a negative charge and the one that loses electrons a positive charge. Considered minutely, a normal atom or molecule that gains an electron is a negative ion, and one that loses an electron is a positive ion. The transfer of electrons or ions by contact and separation is often facilitated by rubbing and friction. Positive and negative charges of electricity produced and kept apart by non-conductors are virtually at rest; that is, they are static. However, owing to their difference of potential, they are acted upon by a force that tends to unite them. This reunion will take place instantly if a low-resistance circuit is provided. It will occur in any event, because there are no perfect insulators. Charges acquire voltage or potential in proportion to the amount of work or energy required to separate them. Stress in the electric field or region around charged bodies is manifested not only in the attraction of opposite charges, but also in a repulsion of charges of like kind. As this effect is elemental, static charges in the aggregate are self-repellent and thus normally reside only on the external surfaces of electrified objects. Although static charges produced in operating rooms often have high potential, they are always extremely small in quantity compared with the most meagre demands of power electricity.

Although static electricity usually develops on non-conductors, a charge can be readily transferred to and stored on insulated conductors. Sometimes this is accomplished by subsequent intimate contact of large surface areas or by slow leakage from one body to the other. More often the transfer of electrons is apparent and the charge exhibited by the conductor is the result of an action known as induction or influence. It is important to know that charges are not produced or lost singly. A positive charge implies an equal negative charge. If the complementary charge seems to be lost or unnecessary, the circuit is simply longer or the phenomenon more involved than was suspected. Positive elemental charges are virtually immobile, except in gases and liquids; and if a positive charge on a body is to be moved, the body upon which it resides will have to be moved with it. In general, therefore, it is well to think of the transfer of electrons or negative charges rather than of positive charges, to regard the appearance of a positive charge as evidence that a negative charge has moved away, and to understand that the removal of a positive charge is due to the invasion of an equal negative charge. Thus, when charges are neutralized or grounded, they are not annihilated; they are permitted to assume merely a close atomic association such as they had before initial separation. However, in this process charges lose energy, and their potentials are reduced virtually to zero. Static electricity of high tension on an insulated conducting body, such as a metal stand with ordinary rubber casters, or a person wearing non-conductive rubber shoes, can discharge through the air if another conductor of considerably different potential is brought near. Such a discharge or spark, even though sometimes too small to be seen or felt, may contain more than enough thermal energy to ignite sensitive explosive mixtures of anæsthetic gas and oxygen.

Static Electricity in Hospitals.

Static electricity is a major cause of fires and explosions in hospital operating rooms and associated anæsthetizing locations. The equipment in operating rooms of most hospitals today includes much electrically non-conductive material that readily acquires electrostatic charges through handling. Many floors are made of highly resistant material that impedes the flow of electricity and prevents proper neutralization of charges. As a result, sparks of ignitable energy often occur in the vicinity of explosive mixtures of combustible anæsthetic gases or vapours. Sparks have occurred at the edge of a breathing mask when it was touched for adjustment by an attendant. It seems likely, from post-explosion inspection, that small spark discharges may have occurred occasionally at barrier points inside anæsthesia machines when rubber bags or breathing tubes were handled or large high-potential charges developed near by.

One obvious way of preventing the development of static electricity would be to eliminate non-conductors, and this method should certainly be employed whenever possible by finding substitutes for easily electrified materials. Cotton sheets, cotton clothing and other definitely essential non-conductors can be regarded as safe if all conducting bodies they may touch or be near have suitable means for the rapid escape of acquired charge. Sparks will not occur if there are better means for neutralization of charges. Castors, wheel tires, stool leg tips, anæsthesia machine bags, breathing tubes, face masks, operating table mattresses and the shoes of personnel therefore should be of conductive rubber or other conductive material or be bridged by suitable conductors. To ensure the neutralization of all charges, conductive paths should be continuous or merge with others. Inasmuch as operating room personnel and almost all furniture make some contact with the floor, it is a matter of convenience and importance that the latter should be conductive. A suitable conductive floor is one that always has a resistance low enough to remove or bring about the safe neutralization of charges at a rate considerably greater than the rate at which they can develop on operating room furnishings or personnel, yet high enough to prevent sparks or shocks from electric power lines or equipment that might become defective. In other words, the floor resistance should lie somewhere between an upper and a lower limit of safety.

The Present Investigation.

The authors carried out a survey of 78 operating rooms, 22 delivery rooms and 16 corridors. Detailed inspections and electrical measurements were made, and appropriate tests were carried out, with the cooperation of operating room personnel. The abundant occurrence of static electricity in

operating rooms was clearly proved, and the efficacy of such recommended measures as could be applied was tested. Laboratory studies confirmed some observations. Numerous test details are provided in the report to show the real magnitude of the electrostatic problem, and to give every hospital some understanding of what its own hazards may be. The authors express the hope that the facts and considerations presented will stimulate an interest in hospital circles for independent study and research and so render minimal a hazard which, up till now, is regarded as having been serious in most hospitals.

Specific Conclusions.

In the light of this investigation the authors have reached the following specific conclusions:

1. In the average operating suite there are many items of non-conductive material that singly or in combination permit and encourage the development of static electricity.

2. The presence of static charges can give rise to incendiary sparks and is a constant threat to patients and personnel in anæsthetizing locations where combustible gases are administered.

3. Many anæsthetic gas mixtures, particularly those rich in oxygen, are highly explosive and easily ignited by static sparks. Some of the commonly used mixtures can be ignited by extremely low energy sparks of the order of 0·001 millijoule—less than a millionth of a gramme-calorie.

4. There are a number of simple ways of preventing the development of static electricity in operating rooms, the most important being the substitution of articles of electrically conductive material for those of non-conductive, charge-producing material. Whether or not all of these substitutions are made, conductive floors and conductive contacts from equipment to floors should be provided to take care of any exigencies, such as the possible introduction into the operating room of some piece of unapproved material electrically charged or likely to be become charged.

5. In operating suites that still have easily charged material lying around, the quantities of induced charge apt to be produced and the potentials involved are such that neutralization can be brought about satisfactorily by conducting paths of fairly light resistance.

6. Floors and shoes of unnecessarily low resistance may give rise to spark and shock hazards in rooms where there are ordinary electrical appliances and portable lamps.

7. The use and proper installation in anæsthetizing locations of electric lamps, motors, plugs and receptacles that carry a third wire for positive grounding would reduce greatly the chance of personnel or patient receiving electric-power shock.

8. The correct amount of resistance in static-charge neutralizing or ground circuit can be determined with adequate margins of safety from a knowledge of the rate of development of charge potential. Dangerous charges commonly require more than 0·1 second to develop.

9. As charge removal accompanies charge development on ground-connected personnel and equipment, conductive paths capable of removing or permitting neutralization of 99% of any probable charge in 0·01 second will give a large practical margin of safety. Neutralization of developing charges on personnel or equipment in operating rooms or other anæsthetizing locations can be adequately and safely accomplished in circuits of several megohms' resistance.

10. Although relative humidities as high as 65% or 70% may not be expected completely to prevent dangerous charging of some types of non-conductive rubber, plastics and synthetic fabrics, assured humidities as low as 50%, relative, will greatly impede the development of charge on cotton and other notably porous materials. Good ventilation will tend to disperse and dilute pockets or strata of explosive gas mixtures and thus generally reduce the danger of ignition.

11. Application of preventive measures must be thorough to assure complete removal of the static electricity hazard from anæsthetizing locations.

Specific Recommendations.

The authors submit specific recommendations, which they describe as minimal for the correction of static and other closely associated electrical hazards. They state that these recommendations recognize the fact that many approved and desirable conductive materials and other items are not available at the present time and that many hospitals cannot undertake the immediate reconstruction of all hazardous areas. The recommendations are as follows:

1. Wool blankets, plastic sheets and most of the usual synthetic-fabric materials should not be used around anæsthetic-gas equipment or patients anæsthetized with combustible-gas mixtures. Cotton blankets and sheets are satisfactory, but if these are stored in a warming compartment some means should be provided to keep them from losing moisture. Before new types of materials are admitted to operating-room or delivery-room suites, they should be rigorously and competently tested under conditions of low relative humidity to be sure that they cannot readily develop high-potential charge.

2. Conductive rubber mattresses, pads and pillows should be substituted for the ordinary variety as soon as they are available. Conductive mattresses are strongly recommended for carriages, especially where non-conductive floors are still in use. Conductive covers are satisfactory if they completely and permanently enclose the non-conductive items. Conductive cover material is becoming available and should be put to use speedily.

3. Personnel wearing ordinary rubber-soled or synthetic-soled shoes may carry static, regardless of the type of floors. Conductive shoes, therefore, should be worn by all personnel who work around combustible anæsthetics or anæsthetized patients. Such shoes should have a resistance of not less than 0·1 megohm each, but they should not have or acquire an individual resistance of more than 0·5 to 1·0 megohm. Until approved conductive shoes can be obtained, leather shoes, unless they have rubber insoles or waterproofing, will usually suffice to bring about neutralization of body charges quickly. If the leather soles are reasonably conductive and recommendations 1, 5, 6 and 8 have been put into effect, the hazard introduced through the use of ordinary rubber or composition heels may be regarded as insignificant.

4. Suitable conductive-rubber breathing tubes, masks and bags should be installed on existing anæsthesia machines as soon as they can be obtained; they should be standard equipment on all new machines.

5. Conductive floors should be used in all operating and delivery rooms and in other rooms where combustible anæsthetics are administered. An effort should be made to keep floors within the limits of present code requirements and well above the lower limit. The opinion of the authors, based on many tests and considerations, is that the most satisfactory well-seasoned floors will introduce, in any neutralizing circuit or to the ground, a resistance of not less than 0·2 megohm or more than 2·0 megohms. Such floors will remove static charge adequately from any conductive bodies properly connected to them and prevent disconcerting, if not dangerous, shock due to possible defects in electrical equipment such as lamps and heaters.

6. Stools with smooth, rounded feet and bare-metal tops are the most satisfactory ones electrically. If upholstered covers are needed for comfort or to prevent sliding or falling, they should be of conductive material. If stool tops are painted or enamelled, these coatings should be removed. Wide cross straps of adhesive tape, sometimes used to prevent sliding, are not objectionable, but at least 50% of the bare top surface of the stool should be left exposed.

7. Non-conductive castors, tires and stool-leg tips should be replaced by conductive rubber or other suitable material on all equipment used in the administration of combustible anæsthetics or in the handling of anæsthetized patients. If these cannot be obtained from the manufacturers of hospital supplies, wet towels to ensure removal of static electricity from operating table, anæsthesia machine, stool and anæsthetist should be used. Until it is possible for a hospital to install conductive floors in all hazardous areas, it is advisable to use wet towels in any instance, as they are much more effective in conducting electricity into floor materials of high resistance than any other method; wet towels can also be used effectively on carriages. If one-megohm resistance type intercouplers are employed they must be kept in good repair and tested frequently.

8. Outer garments of wool, silk or synthetic materials, such as rayon, nylon, orlon et cetera, should be prohibited in anæsthetizing locations. However, there seems to be no substantial evidence that personnel acquire static charge potentials as a result of wearing properly covered undergarments of these materials. Cotton uniforms are more suitable from an electrical standpoint than those of other materials because they retain a useful degree of conductivity at fairly low humidities and because they are not apt to produce or acquire charge by frictional contact with other cotton articles, such as sheets, bandages, sterilized bundles et cetera.

9. Receptacles and plugs that cannot be pulled apart accidentally should be installed where needed. Unless they are of the explosion-proof type they should not be placed lower than five feet above the floor or in any location where combustible anæsthetic gases can pass over them or envelop them. Care should be taken to keep ordinary switches and open motors and heaters well out of range of combustible

gas mixtures. Electric wiring and equipment should be in conformity with the latest approved regulations of the National Fire Protection Association for hospital operating rooms wherever possible.

10. A suitable measuring instrument should be installed in a convenient and safe place for testing the conductivity of shoes of all personnel entering areas where explosive gaseous anæsthetics are administered. If conductive shoes cannot be obtained, shoes of leather or other absorbent material usually can be brought to a desirable value of conductivity in a few minutes by standing on a wet pad or piece of wet carpet. A little glycerin or hygroscopic salt, such as calcium chloride, in the water will give the treatment more permanence.

The authors believe that these recommendations for reducing to a minimum static-spark and ordinary electrical hazards in hospital anæsthetizing areas are pertinent, practical and essential.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held on November 26, 1953, at the Robert H. Todd Assembly Hall, British Medical Association House, 135, Macquarie Street, Sydney, DR. A. J. MURRAY, the President, in the chair.

Problems of the Menopause.

DR. C. L. CHAPMAN read a paper entitled "The Management of the Menopause—Artificial and Natural" (see page 273).

DR. S. G. SANDES read a paper entitled "The Management of the Menopause" (see page 274).

DR. R. ST. J. HONNER expressed his appreciation of both papers and was in agreement with Dr. Sandes about the importance of the psychological approach. Even such a small thing as the prescription of a new hat for the patient might help. There was too much tendency to overlook that approach. Dr. Honner said that "environmental adjustment" was a very nice phrase for a long holiday. Dr. Honner had two or three questions to ask. The first concerned the fact that when a gynæcologist had to remove the ovaries from very young women they did not suffer so much from menopausal symptoms as those in the middle thirties; why was that so? The second question was whether it was not a fact that women now had the climacteric at a much later age than previously; also, whether such women were much more prone to carcinoma of the uterine body. The third question was whether, when an attempt was made to conserve the ovaries, they did not degenerate or become cystic within two years.

DR. F. N. CHENHALL said that an interesting point had been raised by Dr. Chapman, that when young women were treated for carcinoma, they did not suffer the symptoms associated with the menopause. That should give the gynæcologists something to think about. Dr. Chenhall said he was surprised that both speakers had neglected the women with definite gynæcological disease. There were a very large number of women who went through life and through the menopause with a few hot flushes and upsets, but whom the gynæcologists never saw at all. Years earlier Gibbon FitzGibbon had pointed out that women who had definite gynæcological disease tended to have a stormy menopause. Dr. Chenhall thought that that point should have been stressed by the speakers. Dr. Chenhall agreed with Dr. Honner that Dr. Sandes had been very kind to women. He pointed out that since the turn of the century women had had a much harder time than before because of the difficulty of obtaining domestic help. At the present time also many were neglecting their homes and going out to work to improve the family income. A lot of those women were now in the relevant age group and the strain was very great. For such people replacement therapy was not so necessary as sedatives.

DR. H. K. PORTER said that the subject was important, and one with which they were confronted nearly every day. The menopause had been spoken of as one of the most therapeutically abused subjects in the practice of medicine. He agreed with Dr. Chapman that when œstrogen treatment was used, the smaller the dose given and the shorter the period for which it was given, the better. There was at the present time a tendency towards overdosage and too long administration. A woman patient in the early forties might have headaches and feel a little hot, and might persuade her medical adviser to give her œstrogens. That might be harmful. Often a sedative would do good. Even Bishop himself said that stilbœstrol had probably done more harm than good, because it had been given in too large a dosage for too long. Sometimes patients who had not been given proper instructions went on taking œstrogens for years, and finally came for treatment because of irregular bleeding. There was no doubt that the longer the period for which œstrogens were taken, the longer they needed to be taken; patients would themselves say that they could not do without them. Gynæcologists had to be very careful. They also had to be careful to see that when a patient consulted them suffering from menopausal symptoms, they did not dismiss her with a prescription for œstrogen; they should carry out a thorough examination. It was an excellent opportunity, because that was a period when many ills began.

DR. F. A. BELLINGHAM said that the mental readjustment of the patient at the menopause was probably more important than treatment with œstrogens. With regard to the œstrogens themselves, Dr. Bellingham said that he had found that the use of the orally administered œstrogens in an elixir caused a good deal more nausea than the other forms of administration. He agreed with Dr. Chapman that ethinyl œstradiol was the best to use. Dr. Bellingham then referred to a small technical point concerning subtotal hysterectomy; he thought that to teach that that operation should be performed was going back to the Dark Ages. To a gynæcologist with the experience and skill of Dr. Chapman it would be just as easy to perform total as subtotal hysterectomy, and he was referring to the able operator who had a choice in his armamentarium. The mortality was just as high from subtotal as from total hysterectomy. Why should a piece of cervix be left, when it might cause trouble later? Two reasons might be given: (i) it might be of some use there; (ii) there was a belief that the residual cervix was not a site for carcinoma. That might or might not be true; but when one cut down a tree one did not as a rule leave the roots in the ground. Part of the cervix might be left in to support the upper part of the vagina; but the paravesical tissue could be left to do that. In his opinion subtotal hysterectomy was unjustified in the majority of cases because the cervix would be of no further use. Dr. Chapman would probably say that it was of use to the husband for successful coitus; Dr. Bellingham believed that it was of no more use to the husband than as if it was not there, and coitus was quite as successful as if the cervix was there. He had seen a number of cervices that had had to be removed later for malignant disease.

DR. JOHN LOXTON said that he had been Dr. Chapman's assistant for the last seven or eight years, for the first part in his public work and later in his private work, and Dr. Chapman practised what he preached. In earlier days Dr. Chapman had had radical views; he had more recently become conservative. Dr. Loxton thought it unusual for a man of Dr. Chapman's long experience to preserve such an elasticity of mind. Dr. Loxton had watched Dr. Chapman conserve more and more ovaries and take more notice of the cervix—not so much the glands as the nerve supply, which he went to considerable trouble to preserve. Dr. Loxton said that although he was a member of the total hysterectomy school, he would not quarrel with Dr. Chapman over that. He had a question to ask. They were all familiar with the patient complaining of post-menopausal symptoms for some four or five or even more years after the menopause. He asked both speakers how long it was reasonable to consider menopausal symptoms or symptoms which the patient attributed to the menopause as being due to œstrogen deficiency, how long one should treat them with œstrogen, and when one should discard œstrogens and treat the patient on psychological or other lines.

DR. CARL JAEDE said that he had been disappointed that the speakers had restricted their papers to the female menopause; he would have been interested to learn something about the recently discovered male menopause. He was not at all sure about the alleged dangers of œstrogens in menopausal symptoms. They were still advised by not only American but English gynæcologists to use them extensively in "cocktail" dosage in menorrhagia, and he had seen more good than harm result. Dr. Jaede asked when menopausal symptoms commenced in women. He said that there had been cases in his practice in which women at the early age of thirty-five years, who were apparently menstruating regularly, had shown signs of menopausal symptoms which had been relieved by œstrogens. Women aged about sixty years might suddenly present themselves and there might be nothing else to account for the symptoms of flushing, which again were relieved by a short course of œstrogens. It would be interesting to know when the actual menopausal symptoms began and when they might see the end of them. Dr. Jaede said that he had not heard of people taking

œstrogens regularly for over a year; people who did so must go and get them from the chemist unbeknownst to the practitioner.

DR. F. P. PIGOTT said that he had two points to raise. The first concerned Dr. Jaede's reference to ethinyl œstradiol. Dr. Pigott said that he had spent some time in Bishop's clinic at the Chelsea Hospital for Women. There, anyone who complained of uterine bleeding was referred to Bishop, who put her on a certain endocrine régime. He believed that a diagnostic curettage should be performed before œstrogens were used. Once that had been done, then the œstrogens had a place in the control of some forms of uterine bleeding. The second point raised by Dr. Pigott concerned dosage at the menopause. He said that there was no standardized, fixed dosage, but an individual dosage for each patient. Most patients were sensitive to œstrogens, and once the effect was being obtained the dosage should be progressively reduced until the minimum effective dosage was reached, and eventually administration should be discontinued altogether.

Dr. Chapman, in reply, referred first to Dr. Honner's question why young women aged less than thirty years who underwent oophorectomy had less severe menopausal symptoms than those who were more mature. Dr. Chapman thought that the reason was probably that women of the earlier age group were not so set in their habits and ways; as women went from thirty towards forty years they became less adaptable in their lives, and were certainly much more intense in their sex fixation. Dr. Chapman thought that the menopause was occurring later, but that was only a surmise. Many young gynæcologists should be working on that and similar problems. The emancipation of women had caused many to carry on much longer in suitable occupations, and fewer women now sat about all day; menopausal symptoms started earlier in those who led inactive lives. Again to Dr. Honner, Dr. Chapman said that years earlier the Manchester school taught that if the ovaries were left, after two years they were of no use. That had not been his experience. If one removed an odd ovary sometimes fifteen years after hysterectomy, violent symptoms of the menopause would follow—so much so that he now left them. If one removed an ovary because of pain and the patient then had an involutional psychosis, one had not done her much good. Dr. Chapman had had experience of removing such an ovary after many years. The work done at the Manchester school was very drastic indeed and had been proved wrong; Bishop himself had carried out many experiments which proved that the ovaries did not deteriorate to any extent because of a reduced blood supply. In reply to Dr. Bellingham, Dr. Chapman said that if a woman had a healthy cervix—for example, in a case of fibroid tumours or some such condition in which it was necessary to perform hysterectomy, the cervix should be left. When it was necessary to remove all tissues—ovaries and uterus—and widespread endometriosis was present, œstrogens could not be used because they would do damage, and one had to rely on sedatives and psychological treatment. Dr. Chapman said he thought that the removal of the cervix made a great deal of difference to a woman's marriage ability. He had examined large numbers of patients who had undergone total hysterectomy, especially those operated on by general surgeons, and the vagina was greatly foreshortened; such women really suffered a great deal. Most general practitioners would agree with what he said; they were plagued by women with short posterior fornices. Dr. Chapman emphasized that it was possible to leave a healthy (not an unhealthy) cervix. Dr. Chapman said that he could not answer the questions asked by Dr. Loxton and Dr. Jaede about the time when the menopause began or ended; but symptoms of œstrogen lack could occur even in quite young women. In reply to Dr. Pigott, Dr. Chapman agreed that the dosage of œstrogens had to be individual, and they should make it so; they should be guided by the smallest amount that would give the patient a sense of well-being and the relief she required. Dr. Chapman said that he had purposely refrained from mentioning the out-of-date belief that œstrogens caused cancer; that was now known to be incorrect.

Dr. Sandes, in reply, said that two speakers had mentioned the variable period during which symptoms such as flushes might persist; they might begin as early as thirty-five years and go on to seventy. As he had pointed out, there had as yet been no correlation between the severity and number of flushes on the one hand and the œstrogen levels in the body on the other. It was impossible to be certain that œstrogen lack alone produced the symptoms. In the great majority of cases they were over in two or three years or something of that sort. The fact that some patients could go on having them to the age of seventy years seemed to show that other factors than the level of œstrogen in the body were at work. Work done in America with placebos seemed to support that contention. When the symptoms began very early or continued very late, they seemed to be due to something in the psychological background rather than to the œstrogen levels in the body. Dr. Sandes said that from time to time they did see patients with psychoses that seemed to be aggravated by the removal of the ovaries; if a patient had a family history of mental disorder and obvious weakness, if there was any doubt whether a diseased ovary should be left or not, it seemed wiser to leave it.

Dr. Murray, from the chair, thanked both the speakers and those who had taken part in the discussion, which had been opened on a searching note by Dr. Honner. The discussion had been mainly confined to the gynæcological section of the meeting, which was a reflection of the fact that the subject was a major source of worry to the gynæcologists. It had been interesting to see agreement on some points and failure of agreement on others. Dr. Chapman's paper had been practical and based on his wide experience, and those present were grateful to him. Dr. Sandes's paper was something to be read and digested thoroughly, and its publication would be welcomed.

A MEETING of the Victorian Branch of the British Medical Association was held on July 1, 1953, at the Royal Melbourne Hospital. The meeting took the form of a series of clinical demonstrations by members of the medical and surgical staff of the hospital.

Heart Block: Stokes-Adams Syndrome.

DR. GEOFFREY A. PENINGTON first showed a male patient, aged sixty-three years, who had been suffering from sudden attacks of loss of consciousness since May 8, 1953. These attacks occurred without any warning and at any time and were unrelated to effort or posture, and slight twitching occurred in some of them. In less severe attacks there was a feeling of warmth or of strangeness, and as attacks continued, he became aware of a warning of the oncoming loss of consciousness for a few seconds. He was known to be hypertensive and had suffered from a chronic duodenal ulcer which had recently bled. When he was examined on May 14, no signs of a causative lesion were found. His blood pressure was 200 millimetres of mercury, systolic, and 120 millimetres, diastolic, and when no control was achieved with "Dilantin" and phenobarbital, lumbar puncture and cerebral angiography (the latter by Dr. J. B. Curtis) were carried out. No abnormalities were detected except a slight increase in the protein content of the cerebro-spinal fluid; the fluid also failed to react to the Wassermann test. During the few days in Bethesda Hospital the patient had relatively few "turns", reported as pallor and slight twitching without any particular localizing tendency. Later he became loquacious and fatuous, entirely altered in personality, and the attacks became frequent and uncontrollable. He was admitted to the Royal Melbourne Hospital on June 12, 1953. A routine electrocardiogram revealed bundle branch block, and Dr. Ian Swain, house physician, noted the presence of bradycardia and suspected heart block. A further electrocardiogram revealed idioventricular rhythm in lead I for three beats, and later the patient was observed during a period of complete heart block. An attack was seen: after eight seconds' asystole he thought an attack was coming on, after thirteen seconds he lost consciousness, and after twenty-three seconds regular pulsations at a rate of 36 per minute were resumed.

Control was poor with ephedrine, 0·25 grain, administered every four hours, even with the addition of "Neo-Epinine". Digitalis seemed to aggravate rather than alleviate the condition. Ephedrine in a dosage of 0·5 grain at two hourly intervals and atropine sulphate, 1/100 of a grain given by injection four hourly, controlled attacks for three days; but ephedrine given four hourly with atropine given orally was insufficient. Adjustment of dosage was still proceeding; but it was pointed out that despite the difficulties in control and the frequency of the attacks, the patient's personality had returned to normal with the omission of the anti-convulsive drugs.

Mitral Stenosis: Valvotomy.

Dr. Penington's second patient, a male, aged forty-seven years, had presented on April 7, 1953, with a history of dyspnœa on exertion, weakness, and loss of two and a half to three stone over a period of twelve months. For three months he had suffered from nocturnal paroxysmal dyspnœa, and during the two weeks prior to his admission

to hospital he had had recurrent hæmoptysis, cough with retching and precordial tightness. He appeared then to be very ill, almost cachectic, with respiratory distress, and there were the physical signs of a large effusion in the left pleural cavity. The cardiac size could not be determined, but typical signs of mitral stenosis were heard on auscultation—accentuated first sound with *crescendo* presystolic rumble and mitral diastolic *diminuendo* bruit at the cardiac apex, and split second sound and opening snap at the left sternal edge. There was slight hepatic enlargement, but no ascites or manifest œdema was detected. No reaction was obtained to the Mantoux test.

Aspiration of the pleural effusion gave relief, but the wasting was so severe that a pulmonary neoplasm was suspected. No evidence of this was found, and Dr. John Hayward, who examined the patient at that time, considered the entire picture due to mitral stenosis. Valvotomy was performed on May 6, and apart from a right-sided pleural effusion the patient's post-operative course was very satisfactory. As was to be expected, auricular fibrillation occurred (on May 10), but the rate was only 94 per minute because of pre-operative administration of digitalis and continued administration after operation. On May 14 administration of ethylidine dicoumarin was begun as a preparation for an attempt to restore normal rhythm with quinidine sulphate; but he reverted to sinus rhythm spontaneously on May 16. A pericardial friction rub appeared on May 18 and a pulmonary infarct in the right lung on May 20, and on May 21 auricular flutter with varying two to one and four to one block developed. The administration of one milligramme of digoxin daily resulted in auricular fibrillation on May 28, and sinus rhythm returned on June 1, when ethylidene dicoumarin was again being administered. A pleural effusion was aspirated from the right pleural cavity on May 23 and some fluid was still present when the patient returned to his home on June 2. On his readmission to hospital for review on July 1 examination disclosed great improvement on the pre-operative state and no dyspnœa with mild exertion; but he still had signs of mitral stenosis and a friction rub at the base of the right lung. At the time of the meeting reexamination to exclude Koch's infection was proceeding.

Cortisone in Asthma.

Dr. Penington then showed an unmarried female patient, aged fifty-six years, who had first been under his care in 1930 suffering from chronic colitis, which, although not manifesting frank ulceration, was of the idiopathic ulcerative type. Moderately good health had been maintained; but during 1941 she developed rheumatoid arthritis, which was quiescent at the time when he again examined her in 1951. On that occasion a prolonged febrile illness had been associated with hepatic enlargement, and hepatitis of uncertain ætiology was the ultimate diagnosis. In October, 1952, *status asthmaticus* necessitated her admission to hospital, and because of inadequate control with antispasmodics —adrenaline, aminophylline and the like—ACTH was given in doses of 10 milligrammes by the slow intravenous drip method on each of three consecutive days with dramatic relief. The oral administration of cortisone in doses of 25 milligrammes followed for several days, and then on its cessation she remained well during a week in hospital. Pericolitis for a period of ten days interrupted convalescence, and after this intolerable asthma—intolerable to herself and her own local physician—made her readmission to hospital necessary. ACTH (10 milligrammes) was again given, followed by daily doses of cortisone (25 milligrammes given orally), with prompt response, and the oral dosage was gradually reduced to half a tablet each day, then each second day. Cortisone was given for a total period of three months. For two months prior to the meeting no treatment had been necessary. The patient felt comfortable and well, and there had been no withdrawal symptoms.

Dr. Penington stressed the fact that ACTH and cortisone had been used only because of the poor response to the usual lines of treatment and the complicating factors of quiescent chronic colitis and rheumatoid arthritis. Minimal doses had been used, and it had been hoped that withdrawal of the cortisone would be possible without serious rebound; but in view of the frequent need for continued and continuous administration, this outcome had been recognized as a further hazard. ACTH in such a small dose was effective because of the slow rate of administration—10 milligrammes in eight to ten hours—and certainly it had produced a response unequalled by any other procedure in this or other cases. Cortisone and ACTH were effective remedies, but were not curative, and the common experience was a need for almost continuous administration in severe cases.

Waterhouse-Friderichsen Syndrome.

Dr. Penington's next patient was an unmarried girl, aged twenty-one years, a normal, healthy, pretty young woman who had made a complete recovery from classical Waterhouse-Friderichsen syndrome. When walking in the city at lunch-time on March 30, 1952, she had noticed some shooting pains in the left arm and left buttock; but it was not until the early hours of March 31 that she became really ill and was examined by a medical practitioner who reported that she had had a sore throat, headache and pyrexia (temperature 102° F.) and a red patch on the upper part of the abdomen. About six hours after the patch had been noticed she took three "Sulphatriad" tablets which she retained; but as the day progressed so did her illness, and severe persistent vomiting commenced at midday. When she was admitted to the hospital at 9.35 p.m. she was semicoatose, collapsed, and cyanosed, with a pulse rate of 144 per minute and a systolic blood pressure of 40 millimetres of mercury. Photophobia, neck stiffness and widely distributed large purpuric patches (maximal on the abdomen, legs and arms) were evident.

Immediate resuscitative measures were applied, and while one house physician set up the intravenous apparatus, another collected the various medicaments decided upon. At 10.15 p.m. one litre of serum was given, followed by three litres of blood, and five mega units of penicillin were given intravenously and 2·5 mega units intramuscularly. At 10.30 p.m. lumbar puncture produced opalescent fluid: 20,000 units of penicillin were given intrathecally. Cortisone, 250 milligrammes, was given intramuscularly, and "Methedrine", 30 milligrammes, intravenously. At 11.15 p.m. desoxycorticosterone glucoside ("Percorten", water-soluble) was given in a dose of 50 milligrammes intravenously and 50 milligrammes intramuscularly. At 11.45 p.m. the systolic blood pressure was 60 millimetres of mercury, and at midnight 90 millimetres of mercury, the pulse rate being 130 per minute.

The continuation treatment was as follows: cortisone, 100 milligrammes, was given intramuscularly daily; penicillin G, 500,000 units, was given intramuscularly every three hours; "Percorten" (water-soluble), 20 milligrammes, was given intramuscularly every four hours; saline solution and glucose solution in distilled water were given alternately by the intravenous drip method, one litre every six hours; lumbar puncture was performed daily, and 20,000 units of penicillin were given intrathecally. Specimens of blood and cerebro-spinal fluid and from the purpuric patches were taken for cultural examination; no organisms were seen in the cerebro-spinal fluid, which was turbid and contained predominantly polymorphonuclear cells with a few monocytes, lymphocytes and erythrocytes.

At 11 a.m. on April 1 the patient was able to talk; her blood pressure was 84 millimetres of mercury, systolic, and 65 millimetres, diastolic, and her pulse rate was 128 per minute. Oliguria was noted. Vomiting had ceased.

Because of continued improvement, in order to obviate parenteral therapy, and because of their efficacy in meningococcal infections, it was decided to try to give sulphonamides on April 2; but a trial dose of sulphadiazine caused vomiting and distress, so no further doses were given.

On April 3 reduction in the doses of cortisone, "Percorten" and penicillin commenced, and by April 6, when the blood pressure was 140 millimetres of mercury, systolic, and 90 millimetres, diastolic, and slight œdema was noted, the administration of "Percorten" was stopped. On April 7 cortisone therapy was stopped. The cerebro-spinal fluid was normal on April 8, the purpuric patches were rapidly clearing, and medication ceased. The patient left hospital, well, on April 19.

Dr. Penington said that no pathogenic organisms were isolated on attempted culture and the diagnosis of meningococcal septicæmia was therefore unconfirmed; but the clinical picture left no doubt in his mind, and the inability to cultivate organisms from blood and cerebro-spinal fluid increased the evidence in favour of the meningococcus being causative. As he had pointed out, the initial dose of sulphonamide probably destroyed the evidence, but perhaps was of importance in saving the life of the patient. When the patient was asked about any disturbance resulting from cortisone, it was elicited that the first menstrual period after the illness had been delayed and slightly abnormal, but subsequent menstruation was normal. She had resumed her work, and volunteered that she had even been able to catch up on the gossip in her office.

Miliary Tuberculosis.

Dr. Penington next showed a married woman, aged twenty-nine years, whom he had first examined on December 16, 1952, when she was referred because of a history of loss of energy since the birth of her second child five months earlier, and a cough present for five weeks. X-ray examination on December 3 revealed fine mottling in both lung fields, but there had been no reaction to the Mantoux test.

Examination revealed a few post-tussive fine crepitations at the apices of the lungs anteriorly and at the apex of the right lung posteriorly, but no other abnormal signs, and further films of the chest on December 16 confirmed the presence of miliary mottling of both lung fields, which Dr. E. R. Crisp considered was most probably due to hæmatogenous dissemination of tuberculosis.

She was admitted to hospital on December 20, and the Mantoux test failed to produce reactions with tuberculin up to one in 100 or with P.P.D. Gastric lavage was performed on three occasions and the washings were sent for cultural examination for *Mycobacterium tuberculosis*, as was a twenty-four hour specimen of urine. The cerebro-spinal fluid was examined and found to be normal. The erythrocyte sedimentation rate was 54 millimetres in one hour (the maximum fall was nine millimetres in five minutes). The peripheral blood was normal, and no pronounced pyrexia was observed (the maximum temperature was 99·6° F.).

Because of the history and radiological findings, and because of previous experience of proved tuberculous meningitis and eventual death occurring in a patient who remained "Mantoux-negative" throughout his prolonged illness even though his nutrition was always good and pyrexia was never severe, Dr. Penington decided to commence treatment without waiting with streptomycin, 0·5 gramme given by injection twice daily, and para-aminosalicylic acid, 4·0 grammes given three times daily by mouth.

Serial X-ray films were taken, and on January 27, 1953, after five weeks of treatment, there was evidence of decrease in the density of the mottling. Daily administration of streptomycin was continued till February 14, and then the dose was reduced to three days per week and after one month to 0·5 gramme twice weekly; this had been continued with the daily administration of PAS. Rest in bed was continued until July 2, after which limited activity was permitted. The last X-ray film of the chest on June 24 showed normal appearances. The erythrocyte sedimentation rate had improved to nine millimetres in one hour. There was no reaction to the Mantoux test, which was repeated at this time. It was decided to continue the bi-weekly injections and daily administration of PAS for a further period of six months.

Dr. Penington said that all cultures had failed to demonstrate tuberculosis, and therefore the diagnosis was unproven; but the X-ray appearances were so characteristic that it was impossible to exclude a tuberculous cause and unjustifiable to withhold appropriate chemotherapy. In the earlier example of miliary tuberculosis referred to, streptomycin and in fact any restriction of activity had been withheld by those supervising the patient because of no reaction to the Mantoux test, even though there were large hilar shadows and a fine miliary sowing in the lung fields. Dr. Penington had examined that patient when he developed lesions due to the onset of meningitis, which was the first indication of the serious significance of the pulmonary signs. *M. tuberculosis* was isolated from his urine, and autopsy confirmed tuberculosis as the cause of his mediastinal, pulmonary and meningeal lesions; the Mantoux response had remained negative throughout his illness.

As a further illustration of the protean manifestations of tuberculosis, Dr. Penington showed the films of a young woman, who had presented originally on August 20, 1950, when aged eighteen years, with acute thyroiditis which responded to penicillin given for eleven days. Pyrexia slowly subsided during this period and she was well on leaving hospital. Within two weeks pyrexia recurred, and when she was readmitted to hospital on October 9, 1950, she had been febrile with a temperature of 102° to 103° F. for two and a half weeks. A loud systolic bruit was heard along the left sternal edge, maximal at the third rib, and after a short period of observation, during which blood had been taken for culture on three or four occasions, large doses of penicillin were given in case bacterial endocarditis was present. No response occurred even when 8,000,000 units were given daily, and a second examination of the films of her chest disclosed a suspicious area at the right subclavicular region. A film taken with the patient in the lordotic position confirmed the presence of an opaque area measuring 1·0 by 1·5 centimetres in the second left intercostal space. The Mantoux reaction to old tuberculin (one in 1000) was strongly positive. Cultures were set up, and streptomycin (1·0 gramme) was then given alone twice a day, with subsidence of pyrexia in five days and the return of a sense of well-being. Lumbar puncture was performed, and streptomycin was given intrathecally as a prophylactic measure twice a week for one month, on the assumption that the syndrome was due to a miliary spread coincident with the development of the primary lesion. The intramuscular administration of streptomycin was continued with difficulty for three months, a needle phobia having developed. Serial films had shown progressive "healing" of the lesion, and on June 22, 1953, the small opaque area in the right upper zone was smaller and denser, and probably contained a little calcium. The patient was quite well.

Surgery in Ulcerative Colitis.

DR. A. E. COATES presented a series of patients showing the late results of the surgical treatment of ulcerative colitis. All the patients had been referred by physicians and had been under medical treatment for varying periods.

The first patient, an unmarried woman, aged thirty years, had been admitted to the Royal Melbourne Hospital in March, 1937. She had an eleven months' history of diarrhœa, having had six motions a day and three at night, and the stools contained blood. She responded to medical treatment. She was readmitted to hospital in May, 1938, her condition having much deteriorated. Ileostomy was performed in May. She remained in hospital for one year. X-ray examination revealed a narrow colon, with no haustration. She passed blood *per rectum*. In October, 1940, Dr. Coates performed colectomy. She gained in weight and did well until 1947, when hæmorrhage and the passage of pus from the rectal stump required packing to control the bleeding. In October, 1951, a perineal excision of the rectum was performed. Dr. Coates said that the patient was now well, the ileostomy discharged solid fæces, and she worse a rubber bag with no inconvenience.

Dr. Coates's second patient was a woman, aged twenty-seven years, who had been married for six years. After a miscarriage five years prior to her admission to hospital, she suffered from diarrhœa, passing 12 to 15 stools a day; the stools contained blood and mucus. She was under medical treatment in another hospital. She developed an abscess near the anus, and was in hospital for five months. After that she was at home for one year, and had another miscarriage. This was followed by a recurrence of diarrhœa and severe hæmorrhage *per rectum*, necessitating blood transfusion. Caecostomy was performed, and she remained in hospital for four months. The caecostomy was closed. She then had a baby; she was well throughout her pregnancy except for slight diarrhœa towards the end. Six months later the diarrhœa was severe, and she developed an abscess in the right thigh.

Ileostomy was performed in 1952.

In February, 1953, she was admitted to the Royal Melbourne Hospital. She had a small contracted rectum and a recto-vaginal fistula, as well as a fistula on the back of the right thigh. The thyroid was enlarged. She had persistent tachycardia. In March, colectomy was performed, a small stump of rectum being left low in the pelvis. In April, subtotal thyroidectomy was performed. The tachycardia subsided and she was much better. In June, perineal excision of the rectum was performed. The fistula in the thigh healed. At the time of the meeting she was greatly improved and was rapidly gaining in weight.

The next patient shown by Dr. Coates was a married woman, aged thirty-five years, who had been admitted to the Royal Melbourne Hospital in February, 1946, with diarrhœa and blood-stained stools. Except for a period of eight months after the birth of her second child, she had had diarrhœa continually for three years. She was treated medically for four months in hospital with no success. Sigmoidoscopic examination revealed typical ulcerative colitis.

In June, 1946, ileostomy was performed. She gained in weight and was discharged home, passing one stool *per rectum* every second day.

In March, 1948, she was readmitted to the Royal Melbourne Hospital complaining of colicky pain, and passing blood and mucus *per rectum*. In April, colectomy was performed. She was discharged from hospital in May. Dr.

Coates said that she had gained in weight and looked well. The rectum bled easily, and had some pus in it. He proposed to remove the rectum in September, 1953; it would never be suitable for the restoration of bowel continuity.

Dr. Coates then showed a boy, aged fifteen years, who had been admitted to the Royal Melbourne Hospital in March, 1948, with a history of fifteen months' diarrhœa; he passed 20 stools per day and had lost one stone in weight. A sigmoidoscopic examination and examination with a barium clysma revealed typical ulcerative colitis. Under medical treatment, the diarrhœa subsided.

He was readmitted to hospital in January, 1949, with an exacerbation of the diarrhœa, and passing blood and mucus in his stools. The ulcers were seen on sigmoidoscopic examination. In spite of medical care his condition deteriorated; he required a transfusion of two pints of blood on two occasions.

In February, 1949, ileostomy was performed, and his condition improved.

In June, 1950, colectomy was performed. The colon was completely removed and the stump of rectum oversewn.

In May, 1951, an ileo-rectal anastomosis was performed. Since then he had been well, passing three or four stools per day, which did not contain blood.

Dr. Coates's next patient was a married woman, aged thirty-nine years, who had been admitted to hospital in September, 1948; she had a history of ulcerative colitis of two years' duration, passing three or four stools per day.

In December, 1948, she was readmitted to hospital; she had lost three stone in weight, and was passing blood and mucus in the stools. Ileostomy was performed.

In April, 1949, left hemicolectomy was performed.

In July, 1949, right hemicolectomy was performed. The sigmoid stump was left projecting in the lower angle of the abdominal wound, and a closure by the Paul-Mikulicz method was effected, as described by Sir Hugh Devine, in March, 1950.

In July, 1952, an incisional hernia was repaired. Dr. Coates said that the patient was now overweight, and worked for a canteen and the Red Cross in addition to doing her housework. She passed seven or eight small stools a day.

Dr. Coates next showed a married woman, aged twenty-eight years, who had suffered from diarrhœa with the passage of blood and mucus for six years. She had temporarily responded to medical treatment. In November, 1947, ileostomy was performed. In March, 1948, a small bowel obstruction was relieved by operation. In April, 1948, total colectomy was performed, and in October an ileo-rectal anastomosis was performed. In May, 1949, small bowel obstruction was relieved by the division of adhesions. Dr. Coates said that since then the patient had been well, and was a healthy looking woman.

Dr. Coates finally showed a male patient, aged thirty-three years, who had been in the medical ward in April, 1953, with a history of three years' diarrhœa with the passage of blood and mucus. Under medical treatment his condition settled down, but he continued to pass three or four heavily blood-stained motions a day. Sigmoidoscopic examination revealed typical ulcerative colitis; no mucous membrane was present. In May, 1953, ileostomy was performed, but he lost a lot of blood *per rectum* and was very ill.

In June, 1953, left hemicolectomy was performed. One week later there was profuse bleeding from the defunctional end of the ileum. Left hemicolectomy was performed as an emergency operation to stop the bleeding. At the time of the meeting the patient was doing well, and was a possible candidate for ileo-rectal anastomosis.

Summing up the results in 32 of his cases, Dr. Coates said that 13 patients had had restoration of bowel continuity. Two of them had subsequently undergone an ileostomy, and in one of the two continuity was later restored. Thus 12 of the series had normal rectal control. Three had had the rectum excised. Five had died—one of severe hæmorrhage from the bowel before colectomy was completed, multiple polypi being present, one of pyelophlebitis, one of pneumonia and liver failure, and two of obstruction of the small intestine. With regard to seven of the remaining 15, it was probable that most of them would lose the rectum; but in the younger group Dr. Coates intended to wait some years before taking the irrevocable step.

VICTORIAN BRANCH NEWS.

Special Group on Aviation Medicine.

THE Special Group on Aviation Medicine of the Victorian Branch of the British Medical Association will hold a general meeting and film evening at 8 p.m. on Wednesday, March 3, 1954, at 49 Mathoura Road, Toorak, Victoria. All interested members of the British Medical Association are invited to attend.

Medical Societies.

MELBOURNE PÆDIATRIC SOCIETY.

A MEETING of the Melbourne Pædiatric Society was held at the Presbyterian Babies' Home, Camberwell, on July 8, 1953.

Results of Immunization with B.C.G. Vaccine.

DR. DOROTHEA CHURCH said that in the three years under review (1949-1952) 701 infants under two years of age had been vaccinated with B.C.G. at the Central Chest Clinic. Of those, 41, representing 6%, did not return for their first conversion test in two months, but all except one of the rest gave a positive conversion reaction. Two hundred and thirty returned one year later, and seven of those were revaccinated. Positive reactions were still given by 96%. The remaining 86 returned two years after vaccination and eight of those were revaccinated. The remaining 9% still gave positive reactions. Three years after vaccination 16 returned and four were revaccinated. The remaining 75% still gave positive reactions.

Six children developed regional suppurative adenitis. In three the gland was excised and the wound healed readily. In three the gland was aspirated or incised or ruptured, and the resulting discharge continued for months. There was always a mild adenitis in vaccinated infants, but in some the glands became enlarged and palpable but not suppurative and remained so for the period under review. Twenty vaccination sores were larger than 10 millimetres in diameter.

Dr. Church said that it appeared that excision of a suppurative gland gave the best result and that proper technique in giving B.C.G. vaccine was most important.

DR. JOHN COLEBATCH reported the results of immunization with B.C.G. vaccine at the Presbyterian Babies' Home. He said that his chief contributions were (i) a description of the effectiveness of immunization in early infancy (a period when immunological responses were generally less efficient than in later childhood), the period of observation in some of the cases extending into the fifth year, and (ii) a record of the reactions observed following immunization when the infants were under the closest surveillance, which was possible only in a residential institution.

In all, 43 children had been vaccinated, but six of those were over one year of age at the time. Of the remaining 37 infants, 31 were under six months of age when vaccinated, and 17 were under six weeks of age. Seven had been vaccinated in the first three weeks of life; two of those were premature babies who had been vaccinated before their expected date of delivery. No vaccination had been carried out until observation had shown that the infant was in good health and gaining weight at a normal rate. The dosage of vaccine used for infants under twelve months of age was 0·2 mil given in two injections, each of 0·1 mil, in separate sites.

The result of a tuberculin test, either percutaneous or intradermal, was negative in each case before vaccination, and no known contact with active tuberculous infection had occurred. A follow-up Mantoux test with 1:1000 old tuberculin was possible in only 41 cases; in all of these the test result eventually became positive. The first two infants had been vaccinated over four and a half years previously with only 0·1 mil of imported vaccine, and their Mantoux test results nine weeks later were negative. However, the Commonwealth Serum Laboratories vaccine became available shortly afterwards; and when those infants, aged six months, were revaccinated with it in a dose of 0·2 mil, their Mantoux reactions became strongly positive. Three other infants of various ages were Mantoux-negative six weeks after the standard dosage of 0·2 mil, but became Mantoux-positive within the next few weeks; a fourth infant gave an equivocal response after six weeks, when he was suffering from a dietetic disturbance, but on retesting after another fortnight the reaction was definitely positive. Dr. Colebatch said that

he had therefore made it a rule to defer the Mantoux test until at least eight weeks after vaccination.

An attempt was made to follow up each case with annual tuberculin tests, and in a few cases those had been done at the Tuberculosis Bureau, because its situation was more convenient to the parents. A positive Mantoux test result was obtained after one year in 29 out of 30 cases, after two years in 15 out of 16 cases, after three years in eight out of ten cases, and after four years in two out of five cases. As an indication of the effectiveness of very early vaccination, the following Mantoux reactions were observed in the 21 infants who had been vaccinated in the first two months of life: after one year, positive in all 21 cases; after two years, positive in all nine cases; after three years, positive in four out of five cases; after four years, positive in the only case followed.

Dr. Colebatch said that a local papular reaction developed at each injection site, usually appearing three to four weeks after vaccination. In almost half the cases the papules became pustular and discharged, and in 16% a small ulcer developed, healing as a rule within two to three months. It was interesting to note that a discharging lesion developed in 55% of infants vaccinated after three months of age, but in only 30% of 23 infants vaccinated before that age. In every case some regional adenitis developed, usually reaching its maximum some six to eight weeks after vaccination. In two cases a pectoral lymph gland suppurated and discharged a few months after vaccination. It was doubtful if the child's medical condition was faultless in those cases, for attention to the general health was followed by healing of the abscess in a matter of weeks. In a third case (one of the premature infants) the gland reached the size of a walnut after three months and then gradually subsided.

General reactions due to the B.C.G. vaccination were probably non-existent. From the close observation of the infants living in the babies' home it was true that several had developed some transient vague ill health of minor degree or suboptimal weight gains for a week or two. However, in each of those cases careful scrutiny revealed an adequate explanation in the form of teething or a mild upper respiratory tract infection or a dietetic disorder. Had those minor disorders developed at home it would have been easy for the parents to conclude that they were due to the B.C.G. vaccine. One new-born infant, who had the walnut-sized pectoral gland, developed severe acute thrombocytopenic purpura six weeks after vaccination. It was impossible to exclude B.C.G. as the cause of that; but no record of such a complication had been found in the literature, and there were other possible explanations in the child's previous history and in the mother's own history of purpura.

In conclusion, Dr. Colebatch expressed the opinion that the results obtained by Dr. Church and by himself demonstrated that the B.C.G. vaccine prepared by Commonwealth Serum Laboratories was effective in infants and young children in producing a positive tuberculin reaction which would last for several years, and that the vaccine could be used safely in early infancy, even in the neonatal period.

DR. S. W. WILLIAMS in opening the discussion said that technique was important in B.C.G. immunization. There was no risk in administering B.C.G. to the newborn.

Dr. Williams asked whether streptomycin was of any value in avoiding incision of suppurating glands following B.C.G. administration or in aiding healing after incision.

Dr. Church in reply said that streptomycin had been given to two infants and was ineffective. One would expect that considering the avascularity of tuberculous glands. Excision was preferable to incision.

Dr. Williams then asked for the procedure with those children in whom the Mantoux test result became negative after several years. Did Dr. Colebatch agree that a certain percentage of children failed to develop a positive reaction despite a faultless technique?

Dr. Colebatch, in reply, said that circumstances and environment determined the procedure to be adopted for those children in whom the Mantoux test result became negative. If the risk of infection remained, reimmunization was necessary; otherwise the child ran no more risk than others of that age group, and the decision was the prerogative of the parents. Dr. Colebatch said that those who failed to respond to immunization were very few. In his experience there was none, and in Dr. Church's wide experience, one only. The group was unimportant.

DR. EDGAR NORTH said that some degree of adenitis was inseparable from successful immunization. One had to anticipate a suppuration rate of about 1%, a figure comparable with that of a series of English children. Danish workers considered that the maximum treatment advisable was aspiration.

Referring to Mantoux testing, Dr. North said that it was difficult to define the exact meaning of a positive reaction. Old tuberculin 1:1000 was purely an arbitrary concentration, but a failure to respond to that indicated that there would be no Koch's reaction with B.C.G. A number of children whose Mantoux reactions to old tuberculin 1:1000 had become negative would probably give positive reactions with old tuberculin 1:100.

DR. H. J. SINN inquired about the degree of protection afforded by B.C.G. immunization.

Dr. Colebatch, in reply, said that the infectivity rate of immunized children from a tuberculous household was only 20% of that of non-immunized children.

DR. W. F. H. CRICK asked whether a tuberculous mother should be allowed to breast feed her baby. How early should B.C.G. immunization be commenced, and what time should elapse before the baby was returned to the mother?

Dr. Colebatch, in reply, said that the mother should not be permitted to breast feed her baby. Immunization should be carried out as early as possible, and the infant should not be returned to the mother until immunity was effective and the Mantoux reaction to old tuberculin 1:1000 was positive. The minimum time was two and a half months.

Results of Immunization with Pertussis Hæmagglutinin (H.A.P.A.).

DR. STEPHEN FISHER referred to the paper he had read before the Society in July, 1950,[1] on immunization against whooping-cough and the development of H.A.P.A. (pertussis hæmagglutinin, aluminium phosphate adsorbed). He said that following initial clinical trials efforts were made to secure inclusion of H.A.P.A. in a field trial overseas; those were unsuccessful. It was not considered practicable to set up a field trial in Australia. It was therefore decided to issue H.A.P.A. on request to practitioners on the understanding that they would make their experiences regarding the safety and efficiency of the product available to the Commonwealth Serum Laboratories. Unfortunately, no suitable medium had been found for disseminating the information regarding the availability of the product.

Dr. Fisher said that the approximate amount of H.A.P.A. used could be estimated from the issues. Up to July, 1952, 2000 mils had been issued; between July and December, 1952, 920 mils; and between January and December, 1953, 2230 mils. The total issue, therefore, amounted to 5150 mils. Wastage was estimated at two-thirds of the total issue, and the total amount actually injected at 1700 mils, corresponding to 6800 injections at the recommended dosage of 0·25 mil per injection. It therefore appeared that between 3000 and 4000 children had received injections of H.A.P.A., and it was thought that the majority of those received the full course of two injections.

Dr. Fisher then said that most of the material issued went to private practitioners, but some was sent to municipal councils for use in a total of five immunization campaigns. One of those campaigns was carried out in the Melbourne City Council area by Dr. Philip Gilbert and Dr. Bell Broderick in 1951 and 1952; the results were followed as carefully as was possible within the limits of the organization. The other trials were commenced later, and it was too early to estimate results.

There had been no reports of serious reactions following the use of H.A.P.A., and reactions of a greater than mild degree were unusual. It could therefore be concluded that the product was safe to use. The evaluation of the protective efficiency, however, was more difficult. Reports of clinically suspected cases of whooping-cough in children immunized with H.A.P.A. were followed up in Melbourne; in two cases *Hæmophilus pertussis* was isolated. The disease in both those cases was mild and of about one week's duration. In a third case of similar severity the diagnosis of whooping-cough was accepted, in spite of the negative bacteriological findings, because a contact developed clinically typical whooping-cough. In the absence of controls and data on the incidence of the disease, evaluation of the figures was not possible; it was nevertheless felt that some protection was conferred by H.A.P.A.

In conclusion, Dr. Fisher said that he hoped that, as the product was now supplied to doctors for use in private practice, as well as in immunization campaigns, those interested would avail themselves of it, and that data from which the efficiency of H.A.P.A. could be assessed would accumulate in reasonable time.

DR. H. N. B. WETTENHALL said that he wished to emphasize two points. The first was that a satisfactory antibody titre existed four to five months after immunization. There was not sufficient follow-up to determine the maximum response.

[1] See M. J. AUSTRALIA, 1950, 2: 527.

The second fact worthy of mention was the simplicity of immunization. Only two subcutaneous injections, each of 0·25 mil, were required. A slightly greater volume appeared to have no ill effect. Occasionally reactions occurred. Local reactions took the form of a slight swelling or reddening. Abscesses or necrosis did not occur. General reactions were mild, with slight fever and irritability lasting no longer than one day. The hæmagglutinin required no refrigeration and could be left in a physician's bag.

Dr. Wettenhall said that the suitability of hæmagglutinin for young infants aged two to three months was important in averting pertussis in that age group and made it preferable to standard vaccines.

DR. EDGAR NORTH said that it was important to know the antibody titre in children following hæmagglutinin. In mice it was known that a good titre developed and that protected them from pertussis. However, only a properly controlled field trial could demonstrate its practical effectiveness in children, and that had not been achieved to date.

Dr. North mentioned the combined pertussis, diphtheria and tetanus vaccine. The main advantage was the economy of injections, but that appeared to be outweighed by certain disadvantages.

Immunity to pertussis was needed in the very young, whereas diphtheria was extremely rare in the first year of life. Immunization with the standard type of pertussis vaccine was occasionally accompanied by severe reactions and might discourage the cooperation of mothers in having their children immunized with diphtheria toxoid later. Immunization against diphtheria was safe, sound and effective, but there was good reason to doubt the efficacy of pertussis vaccine. Many workers considered that young infants did not respond to diphtheria toxoid in the first year of life. If it was given during that period with a combined vaccine it was essential that a "booster" injection be given six to nine months later. A "booster" for tetanus could be given at the same time if a triple vaccine was originally used.

Dr. North said that despite many disadvantages there was a definite place for combined immunization. Pertussis vaccine increased the antigenicity of diphtheria toxoid, and probably of tetanus toxoid too. The liquid toxoid in a casein hydrolysate medium was preferable to the adsorbed toxoid, as the risk of sterile abscesses was less; and as in the combined form with pertussis vaccine at least three injections were necessary, the important advantage of decreasing the number of injections was nullified.

DR. S. WIENER said that he had recently used the triple vaccine for immunizing 35 infants. Reactions were minimal. Two developed a transitory pyrexia of 102° F. There was no local reaction. The youngest infant was aged five weeks, and although the Schick test result was negative, presumably as a result of transfer of antibodies from the mother, no reaction occurred.

DR. JOHN COLEBATCH said that, as hæmagglutinin had been used for a short period only, it was impossible to state whether the titre remained sufficiently high to protect the infant over the critical two or three years. Was a booster dose required later?

Dr. Fisher, in reply to Dr. Colebatch, said that the lack of evidence made an accurate answer impossible. Much experimental work was yet to be done, but he was convinced of the importance of continuing the work on hæmagglutinin.

Adoption of Children.

Legal Aspects of the Adoption of Children in Victoria.

MR. J. HAMBLETON, LL.M., said that at Common Law adoption in the sense of the transfer of parental rights and duties in respect of a child to another person and their assumption by him was unknown. In England the *Adoption of Children Act* was passed in 1926, and there was similar legislation in all the Australian States. In Western Australia it had been passed as long ago as 1896, in New South Wales in 1923, in Queensland in 1935, in South Australia in 1925, in Victoria in 1928, and in Tasmania in 1920. The Victorian Act was a short Act of some 19 sections and had been amended from time to time, the most recent amendments being contained in the *Adoption of Children (Amendment) Act*, 1953.

Applications for adoption might be made to the Supreme Court of Victoria or to any County Court, and where all consents stipulated for in the Act had been obtained, a Court of Petty Sessions might grant an order. Practically all applications for adoption were in practice made to the County Court. The applications were heard by the judge in his private chambers in camera, and the following was briefly the procedure. A summons was taken out by the proposed adopters merely to place the matter on record. The proposed adopter or adopters (if more than one) swore an affidavit, the form of which was prescribed in the rules made pursuant to the Act. In that affidavit they set out such matters as the date and place of their marriage, a statement that they had not been divorced or separated *et cetera*, particulars of any prior marriage, date and place of birth of the applicants, position in life and financial standing of proposed adopters, particulars of the issue or the likelihood of issue of the applicants and of any medical opinion that they had obtained as to this, whether the consent of the mother or parents of the child had been obtained and the circumstances of how the adoption came about. The form of consent by the mother or parents of the child was verified by an affidavit made by the person who saw the same being signed, and the papers including an order fixing a date for hearing and appointing a guardian *ad litem* were lodged at the Court for perusal by the judge. The guardian *ad litem* was frequently a matron at one of the children's homes or an almoner, and if known to the Court she was approved without further reference; but if the proposed guardian was someone not well known to the Court from previous adoptions and not a minister of religion, an affidavit by the solicitor was required vouching for the suitability of the guardian *ad litem* to act as such. Where the guardian was not a person accustomed to handling adoptions, a copy of rules 17 and 18 of the Adoption of Children Rules setting out his duties and informing him of the confidential nature of his duties was served upon him together with a notice informing him of the date upon which the case would be heard. Provided that the papers were in order the actual granting of the order was a formality, but the parents and the guardian *ad litem* should orally report the result of his investigation to the judge; however, by leave of the judge the report might be made by affidavit.

In 1953 a radical alteration was made to the Act. Hitherto an adopted child had been placed in precisely the same position as a natural-born child for the purpose of inheritance from its adopted parents either under an intestacy or by will; but so far as remoter relatives were concerned it continued to inherit from its grandparents *et cetera* by will or intestacy or settlement through its natural parents and not through its adopted parents. However, by the 1953 Act the adopted child became for all purposes whatsoever the child of its adopted parents and lost all connexion with its natural parents. That provision was new, and it would be hard to judge its effect. However, it was possible to foresee problems arising in certain cases. Mr. Hambleton then quoted the following example. The son of Scottish or English parents settled in Australia, married and subsequently informed his parents of the births of a number of children. In fact, some of those were adopted children. The mother or father in Scotland or England then died, still domiciled in England or Scotland, leaving the sum of £1000 to "each of my grandchildren". Would the adopted children take equally with those naturally born?

Mr. Hambleton then briefly mentioned the procedure which was followed at the Government Statist's office in regard to adopted children. When the identity of the infant with an existing entry in the register of births was proved to the satisfaction of the Court, the statist marked the original entry "Adopted", and he then entered particulars of the adopted child in a register called "The Adopted Children's Register". The form of that register was laid down in the schedule to the Act and originally made clear that the child was an adopted child, but that form was changed in 1936 and all reference to adoption was deleted. The form of a certificate of birth in respect of an adopted child was different from that which was issued in respect of a child who was the natural-born issue of his or her parents. The form in the case of an adopted child made no reference to the date of marriage of the parents. Mr. Hambleton said that he could see no way in which that difference could be avoided. When only one person adopted, the words "by adoption" were inserted after the name of the adopter. Those words must also be inserted when neither the date nor the approximate date of the birth of the child could be established to the Court.

Section 4 dealt with the qualifications for adopting a child, and it provided that an adoption order should not be made where the applicant was under twenty-five years of age or the applicant was less than twenty-one years older than the infant, but neither of those disabilities was a bar if (i) the applicant and the infant were within the prohibited degrees of consanguinity, or (ii) being of the same sex they were of the same blood, or (iii) two spouses applied, and it was the wife who was under twenty-five or less than twenty-one years older than the infant, or (iv) one of the spouses was the natural parent of the infant. The section also provided that an order was not to be made except in exceptional circumstances where the sole applicant was a male and the infant was a female.

Except in special circumstances an order would not be made upon the application of one of two spouses without the consent of the other spouse.

The matters which the Court was required by the Act to consider were: That all necessary consents had been given, that the order would be for the welfare of the child (and this was the most important consideration for the Court), and that the applicants had not received any payment except such as was approved by the Court.

The receipt of money by parents on adoption or offer of any money was unlawful unless sanctioned by the Court.

The Psychiatric Aspects of Adoption.

DR. JOHN F. WILLIAMS said that the psychiatric aspects of adoption were numerous, and considerable uncertainty still existed regarding many problems. First to be considered was the desirability of adoption under at least three headings.

The first was whether the mother of an illegitimate child should be encouraged to keep it or to have it adopted. The answer might depend on special circumstances—for example, social status and family situation—but it was generally thought that the unmarried mother could seldom offer the child the essential needs for satisfactory development, such as food and shelter, love and stability, as well as recognition of its rights as an individual. Since the child's needs and future development should be the first consideration, suitable adoption generally seemed preferable to care by the mother and also to institutional life.

The second consideration was that the time of adoption should be as early as possible. The disadvantages were thought to be lack of breast-feeding, difficulties in estimating likelihood of satisfactory development, and the possibility that the mother might regret her decision later. However, those did not seem to justify delay and there seemed to be valid reasons for early adoption.

It was doubtful whether breast-feeding by an unwilling and rejecting mother was preferable to artificial feeding by the loving foster mother, and the advantages to the foster parents of early adoption and identification between parents and child from an early date were considerable.

The possibility that the mother might later change her mind should be eliminated as far as possible, and the situation should be clarified very early, at least within a couple of months. An estimation of the potentialities of the child was very desirable but often very difficult, if not impossible, within the first year or two. Adoption could never be guaranteed free of risk, and waiting might be very detrimental to foster parents and child.

In infancy, Gessl's developmental scales and others had very doubtful validity, although they were widely used in the United States of America, and the follow-up had been limited. Therefore the estimation in infancy of probable adult intelligence must remain largely a matter of guesswork in the present stage of knowledge. The intelligence of the parents was probably the best guide but still very unreliable. Difficult birth and resulting spasticity or defect or instability should always be considered. The possibility of the inheritance of such conditions as manic-depressive or schizophrenic psychoses seemed fairly definite if the family tree was known to bear such fruit in abundance; but an estimation of the risk was a matter for skilled assessment, and such factors as an isolated puerperal psychosis or senile dementia could be safely disregarded. Family trees with Huntington's chorea, which presented fairly frequently in Tasmania and Victoria, were to be avoided at all cost. Criminal and immoral propensities were not inherited, although there was evidence that some psychopathic characteristics, such as abnormal electroencephalograms, were transmitted.

Bowlby's World Health Organization monograph on maternal care and mental health had put forth a very strong case that many such tendencies resulted from prolonged deprivation of a stable and affectionate background in infancy. The work had attracted considerable attention for several reasons. The emphasis on infancy as the time when not only very unpleasant but largely irremediable defects of character were created had naturally caused concern.

Bowlby had said: "Although it is a proposition exactly similar in form to those regarding the evil after-effects of rubella in fœtal life, or deprivation of vitamin D in infancy, there is a curious resistance to accepting it."

Some appeared to escape from dire effects, but so did some exposed to tuberculosis-infected milk or the virus of poliomyelitis, and yet no one would dream of wilfully exposing children to those hazards.

The critical period appeared to be from the second half of the first year, and it was claimed that the most adequate mothering could not undo the damage if it was left until two and a half years and possibly even until one year. The results of such deprivation were to be seen typically in the cold affectionless psychopath with criminal tendencies, but also to a less degree in hypomaniacs, hysterics, subjects of anxiety states and depressives, as well as in those with intellectual retardation and impairment of abstract thinking.

The definition of maternal deprivation was not identical with institutional life, for many mothers rejected their children, and some institutions might perhaps give adequate mothering, but there seemed to be little doubt that the institutional child was often severely retarded in both intellectual and emotional development. That had been known for many years, but it was to Bowlby's credit that he had collected and added much information on those points and presented them in a very striking way. How far some of his very wide claims would survive the test of time was to be proven, but he had presented a strong case for investigation and an urgent plea for early and satisfactory adoption.

Dr. Williams said that that led to the third heading, the choice of satisfactory foster parents, which presented many problems. Kanner had said that the attitude of parents might be healthy, unhealthy though remediable, and outright malignant, and it certainly seemed that those in the last group should be omitted from the choice of foster parents. Unfortunately their detection was often a matter of great difficulty, and that difficulty was inherent in the nature of the problem as well as the lack of skilled personnel. To avoid the pitfalls enumerated by Bowlby and others it was essential to discriminate, as any adoption was not the answer to the problem of deprivation.

The motivation behind adoption was always complex, and the desire for a child might result from a variety of very unsatisfactory and largely unconscious motives. It might well be that the motives were wholly normal, but that underlying them was such a degree of emotional instability and immaturity, neurosis, or even psychosis that the mother was unable to make a mature adjustment to the adopted child. Sometimes the foster parents had been over-protected, fearful or rejected children themselves and carried characteristics resulting from that to adult life. They might be seeking a child to prop up their immaturity or perhaps to excuse their own emotional inability to stand up to the stress of pregnancy and confinement or even to sexual intercourse. They might be trying to cement together a marriage which was already on the rocks because of such difficulties, holding out the adopted child as a bait to a dissatisfied spouse. Such motives were surely malignant.

The woman who had herself felt rejected might project that onto the thought of having children; and when allowed, encouraged or persuaded to adopt a child she might find the same rejecting tendency still present. That tendency might be shown as overt hostility and neglect with lack of the cuddling and affection so needed by the infant, but it might also be shown in disguise as perfectionism and dissatisfaction with every trifling error of behaviour or appearance in the child and an attempt to justify that by putting it all down to heredity, wilfulness or ill health. In the last case the poor child was dragged from doctor to doctor with an endless series of petty complaints and an ever-increasing irritation that the cause of the supposed imperfections had not been found. That apparently obsessive drive naturally led to coercion and lack of real affection. Sometimes, however, rejection was shown by over-protection and pampering.

Dr. Williams said that many other examples of unsatisfactory foster parents could be given, such as the aging mother seeking to create again her long-lost son and determined that nothing should disturb that image, the couple desiring a prop and household drudge for their old age, the rigid doctrinaire determined to mould the infant according to fixed rules and regulations, and many others. Unfortunately, such examples existed and their elimination was difficult. The adopted child should not be regarded as cement to an unsatisfactory marriage, or a sop to injured pride, and neither should it be regarded as the sovereign remedy for the hysterical, immature or over-anxious personality. The child should be regarded as an individual with its own imperfections and potentialities, needing love, understanding and security, and fortunately those were often to be found in foster homes.

The adoption of an older child presented special problems, but a realization of the relative permanence of character traits developed in early years should never be forgotten, and hopes of a sudden reclamation of the delinquent child should be tempered with considerable caution if such traits had been present since early years.

In conclusion, Dr. Williams said that it seemed that satisfactory adoption within the first few months offered the best solution of many of the problems of illegitimacy and rejection, although possibly a probationary period of a year or so might be a welcome safeguard.

THE REV. P. L. FORSTER discussed practical aspects in the adoption of children, the result of twenty-five years' experience at the Presbyterian Babies' Home. He disagreed with early adoption of the child as advocated by Dr. Williams. The infant adopted in the first few weeks was denied breast-feeding and commenced life at a disadvantage. Another disadvantage of early adoption was the difficulty in assessing whether the infant was quite normal. Mr. Forster said that he considered that twelve months should be the minimum age for adoption.

Prospective adoptive parents should be interviewed to assess their suitability, with special reference to their ethics, mentality and personal habits.

Mr. Forster advocated special attention for the unmarried mother, so that she could live a healthy and relatively happy life whilst awaiting the birth of her child.

DR. JEANNIE STIRRAT, in opening the discussion, said that it was an advantage to have an exchange of legal and medical opinion on the subject of adoption, and despite Mr. Forster's wide practical experience, she entirely agreed with everything Dr. Williams had said. Dr. Stirrat said that she spoke as a mother of adopted children who had now grown up, as well as a woman working in the psychiatric field.

Mr. Hambleton's contribution was of great value, and it was interesting to hear of the more recent amendments to "The Act" in Victoria. In England until a few years before possessions which foster parents had shared with adopted children were given to the natural parents in the event of the children's deaths.

John Bowlby's World Health Organization monograph "Maternal Care and Mental Health", which Dr. Williams had quoted, brought together valid scientific work from those concerned with the better understanding of mental health. The conclusions were admirably summed up in the phrase: "Mental health depends upon the quality of parent-child relationships."

Dr. Stirrat said that she came of a school which sought for every child a meaningful unbroken relationship with a mother figure for at least the first five years of life. The father too was important in those early years to create with mother and child a triangle of security within which the small girl and small boy could confidently grow to womanhood and manhood.

As Dr. Williams had more than adequately presented the case for adoption, Dr. Stirrat said that she would speak briefly about the mother of the illegitimate baby. The single girl seldom embarked on pregnancy from choice, and her pregnancy should be regarded as a symptom of immaturity or neurosis. The trained worker could give her an understanding of the reason for her predicament and the advantage of psychiatric help. The girl of average intelligence and insight responded well to such an approach, and would often hand over her baby to parent figures who could give the infant a good chance to grow up and live satisfactorily.

Dr. Stirrat said that she agreed with Dr. Williams that a child should be adopted as early as possible. One could observe how the attitudes and responses of babies reared from birth in institutions differed from those of babies who from birth had mother figures on whom they could rely. A young baby was normally greedy and demanding, but gradually changed in relationship with his mother figure, and during the second year of life developed an ability to forgo self-gratification for the sake of his mother. The small baby had grown to a child who could mind about the other person, and if that relationship was not allowed to develop, character defects such as destructiveness could occur. Intimate relationships with parent figures built up more stable and enduring characters than did the training and discipline obtained from institutions. It was important to remember that when considering the subject of adoption. The child who was adopted from an institution at the age of three or four years was not to blame for failing to respond to the constant loving care of good adoptive parents, nor could the fault be attributed to the women who had tended him during his early years. Institutions could give no permanent belonging mother figure, with the result that there was a permanent crippling of the ability to make relationships. A child aged three or four years in an institution might appear very friendly, but there was an ominous lack of discrimination. A child in a normal home setting continued with his play, and weighed up each new adult before embarking on an approach.

Dr. Stirrat said that in the selection of adoptive parents education or even cleanliness was less important than the true quality of motherliness. A large proportion of psychiatric subjects came of obsessionally clean parents. It was advisable to have specially trained workers to select adoptive parents, who often needed skilled help, even when the adopted child had good potentialities. Friends and relatives tended to watch for a bad streak in an adopted child, and behaviour accepted within the natural family was often suspect in the adopted.

A child who had known hurt such as separation in early years tended to tell of that hurt in the pre-verbal language of the child. He might wet his bed, soil his pants, pilfer or destroy, but he was saying in the language of the small child: "Be my Mum from the beginning. Show me that you love me whatever I do; make me feel sure that I will never be sent away." With the right response from the new parent figures the little child language would give place to constructive behaviour, but the wrong response with rejection would cause further hurt and confusion.

Dr. Stirrat concluded by saying that in disagreeing with Mr. Forster she was thinking of the mental as well as the physical well-being of the child.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

THE SUPPLY AND DISTRIBUTION OF LYMPH.[1]

Colonial Secretary's Office,
Sydney,
16 November, 1846.

The Deputy Inspector-General of Hospitals.

Sir,

I am directed by His Excellency the Governor to inform you that in consequence of your letter of the 18th September last His Excellency submitted to the Legislative Council your representation of the necessity of establishing a "Vaccine Institution" in this Colony together with an estimate of the annual expense of maintaining such an establishment amounting to £380.

When, however, the estimate was brought forward, the Council limited the vote to £100, it appearing to be their opinion that an establishment such as was proposed by you was unnecessary and that the sum appropriated by them if allowed to a Private Practitioner, to the Sydney Dispensary, or to the Health Officer would be sufficient to enable either to make such arrangements as would provide for a constant supply and distribution of lymph, and to afford ample remuneration for attendance at certain hours on certain days during the week to vaccinate persons. His Excellency therefore requests that you will report which of these suggestions it would in your opinion be most advisable to adopt.

I have, etc.,

W. ELYARD, JNR.[2]

Correspondence.

MEDICO-LEGAL SOCIETY OF NEW SOUTH WALES.

SIR: Like Dr. W. S. Dawson (M. J. AUSTRALIA, February 6, 1954), I am at a loss to understand why the Medico-Legal Society was allowed to go out of existence. Although a vice-president, I have been unable to find out why this should be. The only information I could obtain was that a legal convention was being held and it was inconvenient to hold meetings of the Society at the same time. To the best of my knowledge and belief no committee meeting passed any resolution dissolving the Society, and one can only assume

[1] From the original in the Mitchell Library, Sydney.

[2] The recommendation of the Deputy Inspector General of Hospitals was that the money be placed at the disposal of the Health Officer (Dr. Savage) and this was done on December 31, 1846.

that someone took it upon himself to ignore the wishes of both professions and allowed it to disintegrate by efflux of time. This can only be regarded as an unwarranted assumption of authority.

I would be only too happy to see the Society revived. It served one very useful purpose in bringing together members of two great professions and thus helping to smooth out any misunderstandings which may have existed between them. I suggest that the two former secretaries, one medical and one legal, meet and discuss the resuscitation of a body which, although *in extremis*, is not yet deceased.

Yours, etc.,

JOHN MCGEORGE.

9 Ormonde Road,
Roseville Chase,
New South Wales.
February 6, 1954.

REGISTRATION OF MEDICAL PRACTITIONERS IN NEW SOUTH WALES.

SIR: It amazes me that the letter from the Secretary of the Medical Board of New South Wales published in your journal of January 16, under the heading "Registration of Medical Practitioners in New South Wales", should have evoked no comment from you or from any of your readers.

Why has the imposition of an annual registration fee become necessary? Who is to receive the £6000 extorted from us this year, and even greater sums in the future? If the recipient be the Board, why has this great income now become necessary? With an initial registration fee of five pounds the Board would already have an income exceeding £1000 *per annum*. I should be surprised if the work involved in maintaining the register exceeded forty man-hours per year, and even if it were ten times that, £1000 would cover necessary expenditure twice over.

But if this guinea per year be an additional tax payable to the State Government akin to the fee demanded for the right to work under compulsory unionism, then why should we pay it at all? What would be the position if all, or a vast number of the medical practitioners of New South Wales, declined to submit to this imposition?

This letter referred to above is the first indication I have had of a fundamental change in our status. Till now our position in the community has been permanent and assured. Now apparently it is to be subject to annual licensing. Is such a change of no importance to us? Why has there been no editorial comment at the time of the amendment of the Act?

Yours, etc.,

WEEKS WHITE.

Leeton,
New South Wales,
January 30, 1954.

THE HISTORY OF GENETICS.

SIR: In a subleader on genetics in your issue of January 30, 1954, there are some terse statements which seem to me misleading. You write that in Russia Mendelism has been denounced as capitalistic. This is not exact. The discoveries of Mendel are acknowledged in Russia to be correct in their own limited sphere. What the Russians say is that to extend Mendelism unduly not only leads to false deductions in genetics, but plays into the hands of those like Goebbels who use false racial theories as political levers.

It is undeniable that Russian science does differ from Anglo-American science over a wide field—for example, in economics, astronomy, neurology, psychiatry, physiology, bacteriology, agriculture *et cetera*. It would, of course, be foolish to conclude either science to be completely correct. Scientists, whatever their political hue, are not immune to error, and the history of science contains many examples of false theories that have been readily accepted and afterwards dropped and of true theories that have only won recognition after a long struggle.

But in evaluating Soviet science, and particularly in genetics, it is well to remember that the basic aim of the Soviet people is to increase their material and cultural well-being. One of their immediate objectives, therefore, is to increase agricultural production both in quantity and quality. As they do not labour under the market difficulties that beset our farmers, nor under the obstacles that private property in land raises, this problem reduces itself for them in the main to gaining knowledge of soil care, to providing the best machinery and to breeding the best varieties. In this matter of breeding it is noteworthy that they study with special care the breeding methods employed in Britain, now and in the past.

It is clear that their political objective does not in any way contradict or hinder, but rather impels the active development of science in this field. And in passing it may be said that this holds for all fields of science.

If any government in the Soviet Union acted as you suggest in your subleader, that is, put hobbles on science, it would obviously be acting against the interests of the Soviet State by hindering its growth in power. I would therefore advise some caution in making statements about the Soviet Union. Even if one is hostile to that State, it would be better not to deceive oneself by painting false pictures of it. Hitler and Goebbels, who, by the way, invented the non-existent Iron Curtain, are outstanding examples of the folly of that sort of thing.

In conclusion, let me add that the story of the disappearance of Vavilov is a mere myth. And let me draw your attention to the fact that a considerable body of scientists in England, France, Italy and even America are supporters of Lysenko and severe critics of the opposing school.

Yours, etc.,

GERALD O'DAY, M.D.

473 Bourke Street,
Melbourne,
February 3, 1954.

THALLIUM POISONING.

SIR: For some time past, experimental thallium poisoning in rats has been under study in this department. The work is far from complete, but some of the results appear worth reporting at this stage, because of possible value in the therapy of poisoning in human subjects.

As part of the programme, numerous substances have been screened for ability to alter the course or mortality of thallium poisoning. For these therapeutic trials our normal procedure is to administer by gastric tube to rats weighing 120 to 180 grammes, thallous sulphate solution in the proportion 30 milligrammes of thallium per kilogram of body weight. This dose is invariably fatal in our colony.

Treatment is commenced after eighteen hours, at which time early signs of poisoning are evident. All treatment is given subcutaneously three times daily until the animal dies or has received ten doses.

If treatment is withheld, most animals die early (thirty-six to seventy-two hours) with profuse diarrhœa as the most striking sign. Animals which receive insufficient treatment, or treatment with a relatively inactive material, or occasionally animals which receive supposedly adequate treatment, may survive this acute stage, but die a few days later with signs of damage to the nervous system—exaggerated reflexes, tremors, muscular spasms.

Thallium shows little evidence of cumulation in rats, and it is difficult uniformly to produce chronic poisoning. Many animals survive frequent large but sublethal doses (for example, 15 milligrammes of thallium per kilogram) without obvious effect; a few may ultimately lose hair or become blind.

Several substances have shown promise of value in treatment, but up to the present thiouracil has been the most useful and certainly merits a trial in the treatment of human thallium poisoning. Thiouracil is effective in thallium-poisoned rats in dosages at least as low as 10 by 64 milligrammes per kilogram of body weight (given over a seventy-two-hour perriod), and much higher dosage can be tolerated.

Although the selection of substances for trial in rats is now based on consideration of chemical structure, it is not yet possible to define the molecular configuration and physical properties necessary for "anti-thallium" activity. That thiouracil is an "anti-thyroid" substance is probably coincidental, for some other "anti-thyroid" substances are effective, others are inactive. Under the conditions described iodide has been found inactive, either alone or in conjunction with other treatment, but the value of iodide for gastric lavage in the first aid treatment of thallium poisoning is not in question.

It is not certain that thiouracil will prove to be the most effective of the substances under trial, and it is not at all certain that it will have any value in human subjects, but

this substance is recommended for clinical trial for two reasons: (a) We have had more experience with thiouracil than with any other substance, and in our colony of rats under the conditions of our experiments, thiouracil has proved strikingly successful. (b) Because of its earlier use in the treatment of thyrotoxicosis, much is known of its effects in human subjects.

It is suggested, therefore, that human subjects acutely poisoned by large amounts of thallium (usually accidental or suicidal) should be treated first by gastric lavage with potassium iodide solution, then with large doses of thiouracil. Quite arbitrarily a daily minimum of three grammes (given in portions two-hourly) is suggested for the first two or three days, followed by 0·6 gramme daily.

For chronic thallium poisoning, a course of, say, three weeks at the ordinary maximal dosage (3·0 by 0·2 grammes per day) is suggested.

It would be interesting to hear of the experience of any physician who may choose to use thiouracil in the treatment of thallium-poisoned patients under his care.

Yours, etc.,

ROBERT J. BARTHOLOMEW.

Department of Biochemistry,
The Prince Henry Hospital,
Sydney.

February 2, 1954.

Obituary.

HARRY STEPHENSON LUCRAFT.

THE Secretary of the Western Australian Branch of the British Medical Association has sent the following appreciation of the late Dr. Harry Stephenson Lucraft.

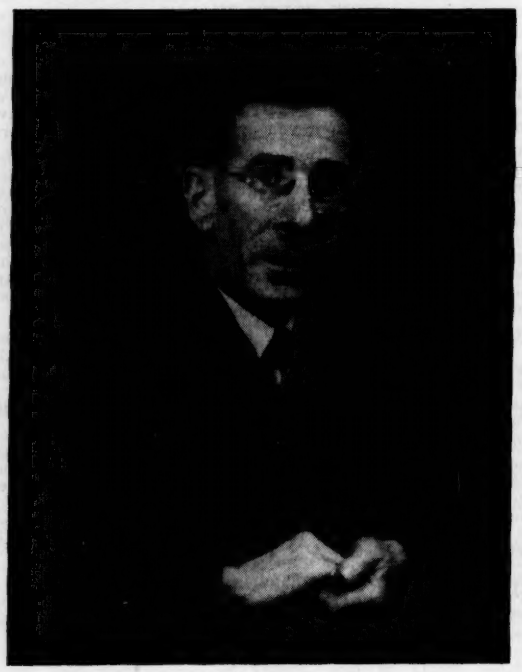
Dr. H. S. Lucraft died in the Royal Perth Hospital on Christmas Eve at the age of fifty-nine years. Some physicians during their lifetime gain the general respect of colleagues and patients. Some—a smaller number—gain admiration as well. A select few win respect, admiration and, in addition, great affection. Of these was Lucraft.

Harry Stephenson Lucraft was born in Adelaide on April 14, 1894. His parents moved to Western Australia shortly thereafter, and Lucraft was educated at Scotch College, Perth. At the age of seventeen years he won a bursary to the University of Edinburgh, where he acquired his medical training. In 1914 on the outbreak of war he volunteered immediately for active service and, along with some of his fellow students, was appointed to duty as a medical probationer on destroyers in the North Sea—a damp, dangerous, exhausting and uncomfortable service. In 1918 after demobilization Lucraft returned to Edinburgh, where, despite his long absence from study, he graduated in 1919 with first class honours and a string of gold medals. After a year on the house staff of the Edinburgh Royal Infirmary he returned to Western Australia and served for two years as district medical officer in the gold-mining town of Norseman. In 1922 he returned to London and, while working for his senior degrees, worked as assistant in a suburban general practice at Dulwich. He acquired the London diploma of tropical medicine and hygiene in 1923 and in 1924 became M.D. (Edinburgh). He then returned to Perth and commenced general practice in an industrial area at Lake Street. He married in 1926 Miss Gladys Steward, of London; Mrs. Lucraft and two daughters survive him.

During the next ten years Lucraft built up a very large practice. At the same time he acquired a reputation as a sound, discerning and intensely human physician with many friends and no enemies. His interests lay always in the field of internal medicine, and in 1928 he was appointed to the Royal Perth Hospital as honorary physician to out-patients.

In 1934 Lucraft returned to London and passed the examination for membership of the Royal College of Physicians—no mean feat at the age of forty after ten years in an exacting general practice. He returned to Perth at the end of that year and rapidly established himself in consultant practice with a special interest in cardiology. His clinical acumen and his utter integrity soon won him the general esteem of patients and colleagues alike, and he was in due course called upon to fill all the offices which fall to the lot of the trusted and able physician. At the Royal Perth Hospital he became honorary physician to in-patients in 1938 and served in that capacity until 1953, when he retired and was appointed honorary consultant physician, which appointment he also held at the Fremantle Hospital. In 1949 he was elected by his colleagues as chairman of the honorary staff of the Royal Perth Hospital; he was re-elected for a further year in 1950. He was a member of the Branch Council of the British Medical Association and was President of the Branch in 1944 and 1945—two difficult years. He was a Foundation Fellow of the Royal Australasian College of Physicians, and acted as deputy councillor in 1951. The Repatriation Department appointed him as consultant physician in 1937, and he served in this capacity until his death. He was a member of the council of his old school, Scotch College, Perth.

When the Second World War broke out Lucraft was appointed as a medical specialist to Western Command. In



1941 he transferred to the Royal Australian Air Force as medical specialist to Western Area with the rank of squadron leader and later of wing commander. As one of the only two physician specialists left in Perth, Lucraft worked extremely hard throughout the whole war period, and the strain of those anxious years undoubtedly took heavy toll of his health and strength.

For many years Lucraft's two chief interests, apart from his work, were photography and the development of the British Medical Association library in Perth. He became one of the most skilful amateur photographers in Australia; his work has been exhibited in London and in Melbourne as well as in his home State. His devotion to the interests of the British Medical Association library became almost a byword in Perth. He took it from the embryo stage, at which it had been left by the untimely death of its founder, the late Dr. Cyril Bryan, and by his enthusiasm and devotion developed it to its present high efficiency. As pleasant hobbies he collected stamps and wrote minor verse with notable fluency.

Above and beyond this record of achievement lives the memory of Harry Lucraft, the man—intelligent, enthusiastic, kindly, loyal and lovable—short in stature, but great in mind and spirit. He will be much missed, and to his family goes the sympathy of the whole of the medical profession of Western Australia.

Post-Graduate Work.

THE MELBOURNE PERMANENT POST-GRADUATE COMMITTEE.

PROGRAMME FOR MARCH, 1954.

Overseas Lecturer.

ON March 10, at 8.15 p.m. at the Medical Society Hall, 426 Albert Street, East Melbourne, Dr. Bradley Patten, Professor of Anatomy in the University of Michigan, will lecture on "Embryonic Heart Action: Micromoving Pictures and Electrocardiographic Studies". He will illustrate his lecture with a film. Dr. Patten is an embryologist and much of his work has centred on the development of the heart, with particular reference to the onset of activity and the electrocardiogram. The fee for this lecture is 15s., payable to the Post-Graduate Committee, but those who have paid an annual subscription to the committee may attend without further charge.

Classes for Higher Qualifications.

Classes have been arranged for candidates for Part I M.D., M.S., D.G.O., D.O., D.L.O., D.P.M., D.D.R., D.T.R., D.A., Primary F.R.A.C.S. and Part I of M.C.R.A.; also classes in pathology for the second part of the diplomas.

Courses will commence on the following dates: anatomy on March 1, at 2.15 p.m., continuing on Mondays and Wednesdays; physiology on March 1, at 3.45 p.m., continuing on Mondays and Wednesdays; pathology on March 8, at 2 p.m., continuing on Mondays and Wednesdays; physics on March 4, at 4 p.m., continuing on Thursdays.

Enrolments should be made by February 15. The fee is £15 15s. per subject, except in the case of the diploma in ophthalmology, when it is £17 17s. for physiology and £17 17s. for anatomy. The fee for Part I D.D.R. is £31 10s.

Course in Surgery Suitable for Candidates for M.S. Part II and Final F.R.A.C.S.

Attention is drawn to the course in surgery which the staff of the Royal Melbourne Hospital will conduct for eight weeks from Monday, March 1. The course will involve five half-days a week and will consist of lectures in surgical subjects, clinical demonstrations, tutorials in surgical pathology and instruction in operative surgery. The Post-Graduate Committee recommends this course.

Enrolments should be made by February 15 with the Post-Graduate Committee.

Country Courses.

Flinders Naval Depot.

A lecture will be given at Flinders Naval Depot at 2.30 p.m. on March 10 by Dr. Alwynne Rowlands.

Hamilton.

The following lectures will be given at Hamilton on March 13: 4 p.m., Dr. John Jens, "Back Injuries with Special Reference to Disk Lesions"; 8 p.m., Dr. Ian Stahle, "Skin Diseases and the Use of ACTH and Cortisone". Inquiries should be addressed to Dr. W. R. Angus, 214 Koroit Street, Warrnambool. Telephone: Warrnambool 52.

Mooroopna.

The following lectures will be given at Mooroopna on March 20: 4 p.m., Dr. Russell Howard, "Acute Surgical Emergencies in Children"; 8 p.m., Dr. Keith Fairley, "Recent Advances in Endocrinology". Inquiries should be addressed to Dr. B. R. Schloeffel, Maud Street, Shepparton.

Warracknabeal.

The following lectures will be given at Warrachnabeal on March 27: 2.30 p.m., Dr. Bruce Anderson, "Obstetrical Emergencies"; 4 p.m., Dr. E. E. Dunlop, "Abdominal Emergencies"; 8 p.m., Dr. Maurice V. Clarke, "Management of Cardiac Emergencies". Inquiries should be made from Dr. J. J. Searby, Warracknabeal.

Fees.

Fees for attendance at country courses are at the rate of 15s. per lecture, but those who have paid an annual subscription to the Post-Graduate Committee are invited to attend without further charge.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED JANUARY 23, 1954.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	2(1)	1	..	..	..	..	..	..	3
Amœbiasis	..	..	..	..	..	..	..	..	..
Ancylostomiasis	5	..	1	..	..	..	4	..	10
Anthrax	..	..	..	..	..	..	..	..	..
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	..	..	1	..	..	..	1
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	1(1)	..	..	..	..	..	..	1
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	4(4)	6(5)	10(7)	..	..	..	..	..	20
Diphtheria	8(7)	7(6)	..	..	3(3)	..	..	..	18
Dysentery (Bacillary)	..	..	1(1)	..	1	..	..	..	2
Encephalitis	..	1	..	..	..	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	..	4(4)	..	..	4(2)	..	1	..	9
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	..	..	..	..	..	..	..
Malaria	..	..	..	..	2	..	..	..	2
Meningococcal Infection	1	1(1)	..	1(1)	3	..	..	..	6
Ophthalmia	..	..	..	..	1	..	..	..	1
Ornithosis	..	1(1)	..	..	..	..	..	..	1
Paratyphoid	..	..	..	..	..	1(1)	..	..	1
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	17(9)	1(1)	1	4(4)	3(3)	..	..	..	26
Puerperal Fever	..	..	..	..	..	..	..	..	..
Rubella	..	16(11)	..	..	19(10)	..	..	..	35
Salmonella Infection	..	..	..	..	1(1)	..	..	..	1
Scarlet Fever	8(4)	17(10)	2(2)	1(1)	..	..	..	..	28
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	1(1)	..	..	..	..	..	..	1
Trachoma	..	..	..	..	1	..	..	..	1
Trichinosis	..	..	..	..	..	..	..	..	..
Tuberculosis	50(37)	31(24)	11(7)	3(1)	6(3)	1	..	..	102
Typhoid Fever	3	..	..	1(1)	1(1)	..	..	..	5
Typhus (Flea-, Mite- and Tick-borne)	..	..	1	..	..	..	..	..	1
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Enrolments.

Enrolments for all courses should be made with the Melbourne Permanent Post-Graduate Committee, 394 Albert Street, East Melbourne. Telephone: FB 2547.

Notice.

UROLOGICAL SOCIETY OF AUSTRALASIA.

THE annual meeting of the Urological Society of Australasia will be held in Sydney from April 5 to 8, 1954. On Tuesday, April 6, at 8.15 p.m., a meeting will be held in the Stawell Hall, 145 Macquarie Street, Sydney, at which the subject for discussion will be "Acute Renal Failure". The speakers will be Dr. Ruthven Blackburn, Director of the Clinical Research Unit, Royal Prince Alfred Hospital, Dr. R. J. Walsh, Director of the Red Cross Blood Transfusion Unit, and Dr. Roger Barnes, of Los Angeles. All members of the medical profession are invited to attend.

Medical Appointments.

Dr. B. F. Venner has been appointed honorary clinical assistant to the surgical section of the Royal Adelaide Hospital.

Dr. H. L. Tonkin has been appointed medical officer, State hospitals and homes, in the Department of Public Health of New South Wales.

Nominations and Elections.

THE undermentioned have applied for election as members of the South Australian Branch of the British Medical Association:

Hawke, John Burton, qualified 1953 (Univ. Adelaide), 219 Stanley Street, North Adelaide, South Australia.

Angus, Barbara Ann, qualified 1953 (Univ. Adelaide), 22 Wheaton Road, Plympton, South Australia.

Evans, Robert George, qualified 1953 (Univ. Adelaide), Box 31, Renmark, South Australia.

Wicks, Graham Ralph, qualified 1953 (Univ. Adelaide), 10 Purnana Avenue, St. Georges, South Australia.

Bailey, Hubert John, qualified 1953 (Univ. Adelaide), 21 West Terrace, Kensington Gardens, South Australia.

Burns, Clement Aylesbury Colin, qualified 1953 (Univ. Adelaide), 111 Prospect Road, Prospect, South Australia.

Carden, David, M.B., B.S., 1953 (Univ. Adelaide), 30 Tusmore Avenue, Marryatville, South Australia.

Markey, Gregory Barton, M.B., B.S., 1953 (Univ. Adelaide) (qualified 1952), 33 Salisbury Crescent, Colonel Light Gardens, South Australia.

Cunningham, Mark Lawrence, M.B., B.S., 1953 (Univ. Adelaide) (qualified 1952), 48 Dutton Terrace, Medindie Gardens, South Australia.

The undermentioned have been elected as members of the South Australian Branch of the British Medical Association: Frederick, Esmond John, M.B., B.S., 1953 (Univ. Adelaide) (qualified 1952); Tipping, Richard Michael, M.B., B.S., 1953 (Univ. Adelaide) (qualified 1952); Steele, Robert Ernest, M.B., B.S., 1952 (Univ. Adelaide) (qualified 1951); Andrew, Ronald Headland, qualified 1953 (Univ. Adelaide); Bennett, Richard Clayton, qualified 1953 (Univ. Adelaide); Broadbent, Ian Nicholas, qualified 1953 (Univ. Adelaide); Elix, Ralph Louis, qualified 1953 (Univ. Adelaide); Cockburn, Andrew Syme, qualified 1953 (Univ. Adelaide); Gaston, Walter Garfield, qualified 1953 (Univ. Adelaide); Hone, Michael Raymond, qualified 1953 (Univ. Adelaide); Jacobs, Donald Arthur, qualified 1953 (Univ. Adelaide); Ligeti, Piroska Magnolina, qualified 1953 (Univ. Adelaide); Messent, Philip William Santo, qualified 1953 (Univ. Adelaide); Mikuzis, Jonas, qualified 1953 (Univ. Adelaide); Paterson, Dennis Craig, qualified 1953 (Univ. Adelaide); Reid, John Douglas, qualified 1953 (Univ. Adelaide); Richards, Maxwell John, qualified 1953 (Univ. Adelaide); Robertson, Colin Frank, qualified 1953 (Univ. Adelaide); Stockley, Henry William, qualified 1953 (Univ. Adelaide); Welch, Howard Walter, qualified 1953 (Univ. Adelaide); West, Rosemary Ruth, qualified 1953 (Univ. Adelaide).

Deaths.

THE following death has been announced:

STEINER.—Peter Steiner, on February 4, 1954, at Sydney.

Diary for the Month.

FEB. 23.—New South Wales Branch, B.M.A.: Ethics Committee.
FEB. 24.—Victorian Branch, B.M.A.: Branch Council Meeting.
FEB. 25.—South Australian Branch, B.M.A.: Scientific Meeting.
FEB. 26.—Queensland Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Victorian Branch (Honorary Secretary, Medical Society Hall, East Melbourne): Associated Medical Services Limited; all Institutes or Medical Dispensaries; Australian Prudential Association, Proprietary, Limited; Federal Mutual Medical Benefit Society; Mutual National Provident Club; National Provident Association; Hospital or other appointments outside Victoria.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Brisbane Associated Friendly Societies' Medical Institute; Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 178 North Terrace, Adelaide): All Contract Practice appointments in South Australia.

Western Australian Branch (Honorary Secretary, 205 Saint George's Terrace, Perth): Norseman Hospital; all Contract Practice appointments in Western Australia. All government appointments with the exception of those of the Department of Public Health.

Tasmania: Part-time specialist appointments for the north-west coast of Tasmania.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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